Barb O'Bryen

4785

Access DB# _____

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: Rebecca Eble (STIC) Examiner #: _____ Date: 5/14/02

Art Unit: 1614 Phone Number 30 _____ Serial Number: 10/019,190 (20028547)

Mail Box and Bldg/Room Location: CM1 2B01 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: _____

Inventors (please provide full names): Jay Kranzler

Earliest Priority Filing Date: 11/5/01

**For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

Please provide structures for compounds of claims 1 & 5 ✓ Search for use of milnacipran 2) use to treat fibromyalgia, pain, chronic fatigue syndrome

Thanks
Rebecca

Point of Contact:
Barb O'Bryen
Technical Information Specialist
STIC CM1 6A05 308-4291

****

STAFF USE ONLY

Searcher: AAB

Searcher Phone #: _____

Searcher Location: _____

Date Searcher Picked Up: _____

Date Completed: 5-31-02

Searcher Prep & Review Time: 60

Clerical Prep Time: _____

Online Time: 38

Type of Search		Vendors and cost where applicable	
NA Sequence (#)		STN	275
AA Sequence (#)		Dialog	
Structure (#)		Questel/Orbit	
Bibliographic	X	Dr.Link	
Litigation		Lexis/Nexis	
Fulltext		Sequence Systems	
Patent Family		WWW/Internet	PDR
Other		Other (specify)	

EIC-1590 (8-01)

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=> fil capl; d que l12; fil medl; d que l19
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FILE COVERS 1907 - 31 May 2002  VOL 136 ISS 22
FILE LAST UPDATED: 29 May 2002  (20020529/ED)

  This file contains CAS Registry Numbers for easy and accurate
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CAS roles have been modified effective December 16, 2001. Please
check your SDI profiles to see if they need to be revised. For
information on CAS roles, enter HELP ROLES at an arrow prompt or use
the CAS Roles thesaurus (/RL field) in this file.


L6             2 SEA FILE=REGISTRY ABB=ON  MILNACIPRAN?/CN
L7           142 SEA FILE=CAPLUS ABB=ON  L6 OR MIDALCIPRAN# OR MILNACIPRAN# OR
                 F 2207
L8           476 SEA FILE=CAPLUS ABB=ON  CHRONIC(2A)FATIGUE
L9           250 SEA FILE=CAPLUS ABB=ON  FIBROMYALGI?
L10         7353 SEA FILE=CAPLUS ABB=ON  PAIN/CT
L11        37165 SEA FILE=CAPLUS ABB=ON  ANALGES?/OBI
L12            2 SEA FILE=CAPLUS ABB=ON  L7 AND (L8 OR L9 OR L10 OR L11)


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 FILE LAST UPDATED: 30 MAY 2002 (20020530/UP). FILE COVERS 1958 TO DATE.

 On April 22, 2001, MEDLINE was reloaded. See HELP RLOAD for details.

 MEDLINE now contains IN-PROCESS records. See HELP CONTENT for details.

 MEDLINE is now updated 4 times per week. A new current-awareness alert
 frequency (EVERYUPDATE) is available. See HELP UPDATE for more information.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2001 vocabulary. Enter HELP THESAURUS for details.

 The OLDMEDLINE file segment now contains data from 1958 through 1965.
 Enter HELP CONTENT for details.

 Left, right, and simultaneous left and right truncation are available in the
 Basic Index. See HELP SFIELDS for details.

 THIS FILE CONTAINS CAS REGISTRY NUMBERS FOR EASY AND ACCURATE
 SUBSTANCE IDENTIFICATION.
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L6            2 SEA FILE=REGISTRY ABB=ON  MILNACIPRAN?/CN
L14          84 SEA FILE=MEDLINE ABB=ON  L6 OR MIDALCIPRAN# OR MILNACIPRAN# OR
                F 2207
L15        2276 SEA FILE=MEDLINE ABB=ON  FIBROMYALGIA/CT
L16        2072 SEA FILE=MEDLINE ABB=ON  FATIGUE SYNDROME, CHRONIC/CT
L17      148093 SEA FILE=MEDLINE ABB=ON  PAIN+NT/CT
L18       18957 SEA FILE=MEDLINE ABB=ON  ANALGESICS/CT
L19           2 SEA FILE=MEDLINE ABB=ON  L14 AND (L15 OR L16 OR L17 OR L18)


=> fil adisalerts; d que l30; fil biosis; d que l33

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FILE LAST UPDATED: 31 MAY 2002 (20020531/ED)


L28          88 SEA FILE=ADISALERTS ABB=ON  MIDALCIPRAN# OR MILNACIPRAN# OR F
                2207
L29       26672 SEA FILE=ADISALERTS ABB=ON  (FIBROMYALG? OR FATIGUE(3A)CHRONIC
                OR PAIN OR ANALGES?)
L30           3 SEA FILE=ADISALERTS ABB=ON  L28 AND L29



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FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 29 May 2002 (20020529/ED)



L6            2 SEA FILE=REGISTRY ABB=ON  MILNACIPRAN?/CN
L31         114 SEA FILE=BIOSIS ABB=ON  MIDALCIPRAN# OR MILNACIPRAN# OR F 2207
                OR L6
L32      161609 SEA FILE=BIOSIS ABB=ON  (FIBROMYALG? OR FATIGUE(3A)CHRONIC OR
                PAIN OR ANALGES?)
L33           1 SEA FILE=BIOSIS ABB=ON  L31 AND L32


=> fil cbnb; d que l36; fil cin; d que l39

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FILE LAST UPDATED: 28 MAY 2002      <20020528/UP>
FILE COVERS 1984 TO DATE.


L34          35 SEA FILE=CBNB ABB=ON  MIDALCIPRAN# OR MILNACIPRAN# OR F 2207
L35        4897 SEA FILE=CBNB ABB=ON  (FIBROMYALG? OR FATIGUE(3A)CHRONIC OR
                PAIN OR ANALGES?)
L36           1 SEA FILE=CBNB ABB=ON  L34 AND L35
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FILE COVERS 1974 - 24 MAY 2002 (20020524/ED) VOL 31 ISS 22

L37 11 SEA FILE=CIN ABB=ON MIDALCIPRAN# OR MILNACIPRAN# OR F 2207
L38 2795 SEA FILE=CIN ABB=ON (FIBROMYALG? OR FATIGUE(3A)CHRONIC OR PAIN OR ANALGES?)
L39 2 SEA FILE=CIN ABB=ON L37 AND L38

=> fil jic; d que l42; fil wpids; d que l45

FILE 'JICST-EPLUS' ENTERED AT 14:01:17 ON 31 MAY 2002

FILE COVERS 1985 TO 28 MAY 2002 (20020528/ED)

THE JICST-EPLUS FILE HAS BEEN RELOADED TO REFLECT THE 1999 CONTROLLED TERM (/CT) THESAURUS RELOAD.

L40 52 SEA FILE=JICST-EPLUS ABB=ON MIDALCIPRAN# OR MILNACIPRAN# OR F 2207
L41 75959 SEA FILE=JICST-EPLUS ABB=ON (FIBROMYALG? OR FATIGUE(3A)CHRONIC OR PAIN OR ANALGES?)
L42 4 SEA FILE=JICST-EPLUS ABB=ON L41 AND L40

FILE 'WPIDS' ENTERED AT 14:01:17 ON 31 MAY 2002

FILE LAST UPDATED: 28 MAY 2002 <20020528/UP>
MOST RECENT DERWENT UPDATE 200234 <200234/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> The BATCH option for structure searches has been enabled in WPINDEX/WPIDS and WPIX >>>

>>> PATENT IMAGES AVAILABLE FOR PRINT AND DISPLAY >>>

>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE http://www.derwent.com/dwpi/updates/dwpicov/index.html <<<

>>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX TOOLS OF THE TRADE USER GUIDE, PLEASE VISIT: http://www.derwent.com/data/stn3.pdf <<<

>>> FOR INFORMATION ON ALL DERWENT WORLD PATENTS INDEX USER GUIDES, PLEASE VISIT: http://www.derwent.com/userguides/dwpi_guide.html <<<

L43 28 SEA FILE=WPIDS ABB=ON MIDALCIPRAN# OR MILNACIPRAN# OR F 2207
L44 30197 SEA FILE=WPIDS ABB=ON (FIBROMYALG? OR FATIGUE(3A)CHRONIC OR

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                PAIN OR ANALGES?)
L45             4 SEA FILE=WPIDS ABB=ON  L43 AND L44


=> fil embase; d que l57;d que l61; fil drugu; d que l66

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L46           214 SEA FILE=EMBASE ABB=ON  MILNACIPRAN/CT
L47          2360 SEA FILE=EMBASE ABB=ON  FIBROMYALGIA/CT
L48          2190 SEA FILE=EMBASE ABB=ON  CHRONIC FATIGUE SYNDROME/CT
L50         37771 SEA FILE=EMBASE ABB=ON  ANALGESIA+NT/CT
L51         18930 SEA FILE=EMBASE ABB=ON  ANALGESIC AGENT/CT
L57             0 SEA FILE=EMBASE ABB=ON  L46 AND (L47 OR L48 OR L50 OR L51)



L46           214 SEA FILE=EMBASE ABB=ON  MILNACIPRAN/CT
L49        187852 SEA FILE=EMBASE ABB=ON  PAIN+NT/CT
L60            94 SEA FILE=EMBASE ABB=ON  L46/MAJ
L61            15 SEA FILE=EMBASE ABB=ON  L49 AND L60


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>>>  SEE HELP COST                                        <<<

>>>  FILE COVERS 1983 TO DATE  <<<
>>>  THESAURUS AVAILABLE IN /CT  <<<



L63        113520 SEA FILE=DRUGU ABB=ON  (FIBROMYALG? OR FATIGUE(3A)CHRONIC OR
                  PAIN OR ANALGES?)
L65           138 SEA FILE=DRUGU ABB=ON  MILNACIPRAN/CT OR MIDALCIPR/CT
L66             7 SEA FILE=DRUGU ABB=ON  L63 AND L65


=> dup rem l19,l42,l66,l12,l33,l61,l30,l36,l39,l45

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PROCESSING COMPLETED FOR L66
PROCESSING COMPLETED FOR L12
PROCESSING COMPLETED FOR L33
PROCESSING COMPLETED FOR L61
PROCESSING COMPLETED FOR L30
PROCESSING COMPLETED FOR L36
PROCESSING COMPLETED FOR L39
PROCESSING COMPLETED FOR L45
L67 35 DUP REM L19 L42 L66 L12 L33 L61 L30 L36 L39 L45 (6 DUPLICATES REMOVED)
ANSWERS '1-2' FROM FILE MEDLINE
ANSWERS '3-6' FROM FILE JICST-EPLUS
ANSWERS '7-12' FROM FILE DRUGU
ANSWERS '13-14' FROM FILE CAPLUS
ANSWERS '15-27' FROM FILE EMBASE
ANSWER '28' FROM FILE ADISALERTS
ANSWER '29' FROM FILE CBNB
ANSWERS '30-31' FROM FILE CIN
ANSWERS '32-35' FROM FILE WPIDS

=> d ibib ab hitrn l67 1-35;fil hom

L67 ANSWER 1 OF 35 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 97081884 MEDLINE
DOCUMENT NUMBER: 97081884 PubMed ID: 8923127
TITLE: Efficacy and tolerability of **milnacipran**: an overview.
AUTHOR: Montgomery S A; Prost J F; Solles A; Briley M
CORPORATE SOURCE: St Mary's Hospital Medical School, London, UK.
SOURCE: INTERNATIONAL CLINICAL PSYCHOPHARMACOLOGY, (1996 Sep) 11 Suppl 4 47-51. Ref: 24
Journal code: ICP; 8609061. ISSN: 0268-1315.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English

FILE SEGMENT: Priority Journals
ENTRY MONTH: 199703
ENTRY DATE: Entered STN: 19970327
Last Updated on STN: 19970327
Entered Medline: 19970319

AB The relative benefits and risks of **milnacipran**, a novel antidepressant which selectively inhibits the reuptake of serotonin and noradrenaline, have been evaluated in comparative trials against tricyclic antidepressants (TCAs) or selective serotonin reuptake inhibitors (SSRIs). A total of 2462 patients with major depressive disorders have been investigated. At the optimal dose (50 mg twice a day), the efficacy of **milnacipran** was equivalent to that of the TCAs, with response rates of approximately 65% in both cases. **Milnacipran** was consistently effective against all of the principal elements of depression (anxiety, cognitive function, sleep and psychomotor retardation), and did not produce sedation or the emergence of suicidal thoughts. The Clinical Global Impression (CGI-3) score, a measure of the overall therapeutic impact of a treatment, was significantly higher with **milnacipran** than with TCAs (1.98 versus 1.84, $p < 0.05$). TCAs were associated with a higher frequency of adverse events than **milnacipran**, particularly with respect to anticholinergic-like effects; dysuria was the only adverse event occurring twice as frequently with **milnacipran** than with TCAs. Compared with TCAs, **milnacipran** was also associated with a lower incidence of cardiovascular adverse events. No haematological abnormalities occurred during treatment with **milnacipran**, and the incidence of abnormal liver function tests tended to be lower with **milnacipran** than with TCAs. In comparisons with SSRIs, **milnacipran** produced significantly higher response rates. The CGI-3 scores were significantly higher in **milnacipran**-treated patients (2.64 versus 2.32, $p < 0.05$). The adverse event profiles of the two treatments were similar, as was the incidence of abnormal liver function tests. These studies suggest that **milnacipran** offers clinical advantages over TCAs in terms of tolerability, and over SSRIs in terms of efficacy. In particular, the lack of cardiovascular adverse events appears to offer advantages in cases of deliberate overdose. To date, 15 such overdoses have occurred; none was fatal and each had a favourable outcome. The reproducible pharmacokinetic characteristics of **milnacipran** present further advantages over both groups of agents, due to lack of drug accumulation and a low risk of drug interactions.

L67 ANSWER 2 OF 35 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 97081883 MEDLINE
DOCUMENT NUMBER: 97081883 PubMed ID: 8923126
TITLE: **Milnacipran** and selective serotonin reuptake inhibitors in major depression.
AUTHOR: Lopez-Ibor J; Guelfi J D; Pletan Y; Tournoux A; Prost J F
CORPORATE SOURCE: Neuva Zelanda 44, Madrid, Spain.
SOURCE: INTERNATIONAL CLINICAL PSYCHOPHARMACOLOGY, (1996 Sep) 11 Suppl 4 41-6. Ref: 32
Journal code: ICP; 8609061. ISSN: 0268-1315.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199703
ENTRY DATE: Entered STN: 19970327
Last Updated on STN: 19970327
Entered Medline: 19970319

AB In drug development the move from tricyclic antidepressants (TCAs) to selective serotonin reuptake inhibitors (SSRIs) involved not only the loss

of the direct receptor interactions responsible for the adverse side effects of TCAs, but also the ability to inhibit the reuptake of noradrenaline. Selectivity for the single neurotransmitter, serotonin, may explain why SSRIs tend to be less efficacious than the TCAs, especially in more serious forms of depression. The advent of selective serotonin and noradrenaline reuptake inhibitors (SNRIs) has tended to confirm the idea that an action on both monoamine systems is important for maximal antidepressant efficacy. This paper reviews clinical trials comparing the new SNRI **milnacipran** with the SSRIs fluoxetine and fluvoxamine. A meta-analysis of the principal trials shows greater response rates (the proportion of patients with a decrease in symptom scores of 50% or more) with **milnacipran** (50 mg twice a day) than with fluoxetine (20 mg once a day), or fluvoxamine (100 mg twice a day) (**milnacipran**: 64%; SSRIs: 50%). Remission rates (the proportion of patients with Hamilton Depression Rating Scores of 7 or below) were also higher with **milnacipran** than with SSRIs (39 versus 28%). In one study, in which 100 mg **milnacipran** was given once a day in the evening, the higher response rate obtained with fluoxetine appears to be largely attributable to an inappropriate **milnacipran** dosage regimen. Data from a pharmacovigilance database including all patients participating in clinical trials with **milnacipran** (n = 5732) showed that, compared with the SSRIs, **milnacipran** produced fewer gastrointestinal side effects, such as nausea, and less anxiety. **Milnacipran** was, however, associated with a higher incidence of headache, dry mouth and dysuria. The results of these studies suggest that **milnacipran** is superior in efficacy to SSRIs and is equally well tolerated. **Milnacipran**, therefore, appears to offer a therapeutic advantage over the SSRIs.

L67 ANSWER 3 OF 35 JICST-EPlus COPYRIGHT 2002 JST DUPLICATE 5
ACCESSION NUMBER: 950051727 JICST-EPlus
TITLE: Clinical Effect of **Milnacipran** hydrochloride(TN-912), a New Antidepressant, in the Field of Psychosomatic Medicine.
AUTHOR: TSUTSUI SUEHARU
KATSURA TAISAKU
KAWANO TOMONOBU
SUEMATSU HIROYUKI
KIKUCHI TAKENORI
KOJIMA KATSUMI
TAIRA YOICHI
SAITO TOSHIJI
OKUMA YUMIKO
CORPORATE SOURCE: Toho Univ., Sch. of Med.
LCCSutoresuigakuken
Morinosato Hosp.
Univ. of Tokyo, Univ. Branch Hosp.
Tokyo Women's Medical College, Second Hospital
Nihon Univ., School of Medicine, Itabashi Hosp.
Kokusai Shinzen Sogo Byoin
Seikokai Koganehara Hosp.
Fukujukai Saitama Soka Hosp.
SOURCE: Rinsho Iyaku (Journal of Clinical Therapeutics & Medicines), (1994) vol. 10, no. 11, pp. 2473-2488. Journal Code: Y0906A (Fig. 5, Tbl. 10, Ref. 9)
ISSN: 0910-8211
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article
LANGUAGE: Japanese
STATUS: New
AB The efficacy, safety and usefulness of **milnacipran** hydrochloride(TN-912) were investigated on depression and depressive state in the field of internal and psychosomatic medicine. The results obtained

are as follows. 1) In FGIR "marked improvement" was 18.9% and combined rate of "moderate improvement" and higher was 62.2%. 2) In OSR "no side effects" was 81.4% and the incidence of side effects that were mainly "drowsiness" and "nausea" was 16.3%(7 patients out of 43). No severe adverse reactions were observed. 3) In GUR "extremely useful" was 16.2% and the combined rate of "fairly useful" and higher was 62.2%. 4) The physical and psychological scores apparently decreased week by week after initiation of the therapy as compared to predosing. 5) In the physical symptoms high improvement ratings were observed in "nausea", "abdominal **pain**", "fatiguability", "dyspnoea", "anorexia", "diaphoresis", "headache/heavy headedness" and "fatiguability generalized". In the psychological symptoms "waking during the night", "insomania, initial", "hypobulia", "enervation" and "depression" were highly improved. As mentioned above, **milnacipran** hydrochloride demonstrated its efficacy on depression and depressive state, which are frequently seen in the field of internal and psychosomatic medicine, with lower incidence of adverse events. Taking these results into consideration, it is suggested that **milnacipran** hydrochloride is a useful therapeutic drug on depression and depressive state. (author abst.)

L67 ANSWER 4 OF 35 JICST-EPlus COPYRIGHT 2002 JST
ACCESSION NUMBER: 1000238896 JICST-EPlus
TITLE: New drug SNRI for depression. Serotonin and noradrenaline reuptake inhibitors. 1. History of the development of the antidepressants.
AUTHOR: KOYAMA TSUKASA
CORPORATE SOURCE: Hokkaido Univ., Grad. Sch.
SOURCE: Iyaku Janaru (Medicine & Drug Journal), (2000) vol. 36, no. 2, pp. 707-710. Journal Code: Z0650A (Ref. 10)
ISSN: 0287-4741
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Commentary
LANGUAGE: Japanese
STATUS: New
AB History of the development of the antidepressants which began with imipramine and iproniazid is outlined presenting the antidepressants under development at present. Selective serotonin reuptake inhibitors (SSRI : 5 types including fluoxetine) have been recently put on the market. In addition, serotonin and noradrenaline reuptake inhibitors (SNRI : **milnacipran**, etc.) of the fourth generation antidepressant have been approved, and clinical trials of the reversible MAO-A inhibitors (moclobenide, etc.) are progressing. The depression treatment in Japan has met large revolution.

L67 ANSWER 5 OF 35 JICST-EPlus COPYRIGHT 2002 JST
ACCESSION NUMBER: 950519543 JICST-EPlus
TITLE: Clinical Effect of **Milnacipran** Hydrochloride (TN-912) in Depression and Depressive States, a New Antidepressant. Dose Finding Study.
AUTHOR: MURASAKI MITSUKUNI; MIURA SADANORI
UESHIMA KUNITOSHI
HASEGAWA KAZUO
ENDO SHUNKICHI
YAMAUCHI TOSHIO
MORI ATSUYOSHI
YAGI GOHEI
CORPORATE SOURCE: Kitasato Univ., Sch. of Med.
Showa Univ., Sch. of Med.
St. Marianna Univ.
Nippon Med. Sch.
Saitama Med. Sch.
Jikei Univ. School of Medicine
Sch. of Med., Keio Univ.

SOURCE: Rinsho Iyaku (Journal of Clinical Therapeutics & Medicines), (1995) vol. 11, no. Suppl 3, pp. 85-101. Journal Code: Y0906A (Fig. 3, Tbl. 10, Ref. 8)
ISSN: 0910-8211
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article
LANGUAGE: Japanese
STATUS: New

AB An open dose-finding study of **milnacipran** hydrochloride was conducted in 82 patients with depression and depressive state. The starting dose for the first 1 week was assigned as 50mg/day or 25mg/day, and from week 2, the dose was apropriately adjusted to the disease conditions. 1) The number of patients subjected to the analysis was 75 except 7 of completely excluded cases. There was no bias in background factors between the two groups. 2) The final global improvement rates were 20.5% and 20.0% assessed as "markedly improved" in the 50mg and 25mg groups, respectively, and similarly 46.2% and 37.1% assessed as "moderately improved" or more, showing a higher rate in the 50mg group, but there was no significant difference. 3) The rates assessed as "no adverse reaction at all" were 75.0% and 74.3% in the 50mg and 25mg groups, respectively, showing no significant difference between the two groups. The incidences of adverse reaction were 25.0% and 22.9% in the 50mg and 25mg groups, respectively, without a significant difference. The major adverse reactions were "thirst", "constipation" and other anti-cholinergic side effects, "nausea", "sleepiness", "headache/dull headache", "irritated feeling/nervousness", etc., but none of them were severe and each of the frequencies was low. The frequencies of abnormal clinical laboratory finding were also low, and no particularly severe one was observed. 4) The general usefulness were 15.4% and 20.0% evaluated as "extremely useful" in the 50mg and 25mg group, respectively, and similarly, 43.6% and 34.3% evaluated as "fairly useful" or more, showing no significant difference between the two groups. From the above results, it was considered that **milnacipran** hydrochloride, starting from 50mg/day followed by increasing up to 150mg/day depending on the disease conditions, is useful in the treatment of depression and depressive state, with less anti-cholinergic side effect. (author abst.)

L67 ANSWER 6 OF 35 JICST-EPlus COPYRIGHT 2002 JST
ACCESSION NUMBER: 950536827 JICST-EPlus
TITLE: Clinical Evaluation of **Milnacipran** Hydrochloride (TN-912) in Depression and Depressive State, a New Antidepressant.
AUTHOR: MURASAKI MITSUKUNI; MIURA SADANORI; TAKAHASHI AKIHIKO; INAMI MITSUAKI; KASAHARA TOMOYUKI
YAMASHITA ITARU; MATSUBARA RYOJI; ODAGAKI YUJI; KOYAMA TSUKASA
CORPORATE SOURCE: Kitasato Univ., East Hosp.
Hokkaido Univ., Sch. of Med.
SOURCE: Rinsho Iyaku (Journal of Clinical Therapeutics & Medicines), (1995) vol. 11, no. Suppl 3, pp. 71-83. Journal Code: Y0906A (Fig. 3, Tbl. 8, Ref. 11)
ISSN: 0910-8211
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article
LANGUAGE: Japanese
STATUS: New

AB A novel antidepressant, **milnacipran** hydrochloride, was given to 47 patients with depression or depressive state, and the following results were obtained. 1) Excluding one completely exclusive case, 46 were subjected to the evaluation. 2) Regarding the final global improvement rate, 10 cases were assessed as "markedly improved", 13 as "moderately improved", 7 as "slightly improved", 9 as "unchanged", 1 as "aggravated" and 2 as "impossible-to-judge", that is the rate of "moderately improved"

or more was 50.0%. 3) The dose was increased from 50mg/day to a maximum of 225mg/day, but any change in the pattern of onset of adverse reactions was not observed. 4) It was indicated that the range of optimum doses was between 50mg and 150mg. 5) The onset of the effect was relatively rapid. 6) By symptoms, generally, favorable effects were observed in all items, particularly, the improvement rates were high in "depression", "Denkhemmung", "malaise" and "headache/dull headache". 7) Adverse reactions were observed in 17 (37.0%) of 46 cases, "constipation" which is an anticholinergic adverse reaction was observed in 13.0%, "thirst" in 8.7% and others observed were "nausea" in 6.5%, etc. (author abst.)

L67 ANSWER 7 OF 35 DRUGU COPYRIGHT 2002 THOMSON DERWENTDUPLICATE 1
ACCESSION NUMBER: 2001-29400 DRUGU P
TITLE: Involvement of brain monoamine receptors in **analgesic** effect of antidepressants.
AUTHOR: Ishikawa Y; Yokogawa F; Ohtsuka N; Nara K; Masuda Y; Hosoyamada A; Oguchi K; Kiuchi Y
CORPORATE SOURCE: Univ.Showa
LOCATION: Tokyo, Jap.
SOURCE: Jpn.J.Pharmacol. (85, Suppl. 1, 221P, 2001)
CODEN: JJPAAZ ISSN: 0021-5198
AVAIL. OF DOC.: Dept. of Pathophysiology, Showa University, Tokyo 142-8555, Japan.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB Licking time after formalin injection into the hindpaw of rats was inhibited by i.p. pretreatment of nisoxetine (NS), imipramine (IM), nortriptyline (NR), milnacipran (ML), maprotiline (MA) and sertraline (SR) in a dose-dependent manner. IM-induced **analgesia** was antagonized by i.c.v. prazosin (PZ) and ketanserin (KT) but not ondansetron (ON). I.c.v. injection of SDZ-205-557 enhanced IM-induced **analgesia**. The results suggest that stimulation of brain alpha-1 and 5-HT receptors which resulted from inhibition of MAO uptake are possibly involved in **analgesic** effect by antidepressants. The brain 5-HT4 receptor is likely to suppress their **analgesic** effect. (conference abstract: 74th Annual Meeting of the Japanese Pharmacology Society, Yokohama, Japan, 2001).

L67 ANSWER 8 OF 35 DRUGU COPYRIGHT 2002 THOMSON DERWENTDUPLICATE 2
ACCESSION NUMBER: 1998-27787 DRUGU T S
TITLE: A double-blind comparison of the efficacy and safety of milnacipran and fluoxetine in depressed patients.
AUTHOR: Guelfi J D; Ansseau M; Corruble E; Samuelian J C; Tonelli I; Tournoux A; Pletan Y
CORPORATE SOURCE: Univ.Paris; Fabre
LOCATION: Paris, Villejuif, Marseilles; Boulogne, Fr.; Liege, Belg.
SOURCE: Int.Clin.Psychopharmacol. (13, No. 3, 121-28, 1998) 2 Fig. 3 Tab. 26 Ref.
CODEN: ICLPE ISSN: 0268-1315
AVAIL. OF DOC.: Department of Psychiatry, Hopital Paul Brosse, 12 Avenue P. Vaillant-Couturier, 94804 Villejuif Cedex, France.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB The efficacy and safety of 2 doses of milnacipran (MLP) and fluoxetine (FXT) were compared in 289 patients with depression in a randomized, double-blind, placebo-controlled trial. MLP was found to be at least as effective and as well tolerated as FXT. The fewest side-effects were seen with the lower dose of MLP and the side-effects associated with both doses of MLP and FXT were abdominal **pain**, constipation,

anxiety, nausea and vomiting, agitation, insomnia, diarrhea, vertigo and headache. There was an increased incidence of tachycardia in the patients treated with the higher dose of MLP and the greatest change in body weight was seen with FXT. The results suggest a slight advantage in the use of the lower dose of MLP in the treatment of depression in terms of efficacy and safety.

L67 ANSWER 9 OF 35 DRUGU COPYRIGHT 2002 THOMSON DERWENT
ACCESSION NUMBER: 2002-11734 DRUGU T S
TITLE: Differential effects of milnacipran and fluvoxamine, especially in patients with severe depression and agitated depression: a case-control study.
AUTHOR: Fukuchi T; Kanemoto K
CORPORATE SOURCE: Univ.Med.Aichi
LOCATION: Aichi, Jap.
SOURCE: Int.Clin.Psychopharmacol. (17, No. 2, 53-58, 2002) 4 Tab. 26 Ref.
CODEN: ICLPE ISSN: 0268-1315
AVAIL. OF DOC.: Department of Neuropsychiatry, Aichi Medical University, 21 Yazako-Karimata, Nagakute, 480-1195 Aichi, Japan. (E-mail: peh06237@nifty.ne.jp). (K.K.).
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB The Authors compared antidepressant efficacy of milnacipran (MIL) and fluvoxamine (FLU) in 192 outpatients with major depression, using the 17-item Hamilton Depression Rating Scale (HDRS). While no significant difference between the treatment groups was found overall, a positive response was recorded significantly more often with MIL than FLU recipients whose baseline HDRS total score was greater than 19 points. There was a significant difference of response for the "agitation" and "insomnia" factors in favor of MIL. In both groups, the incidence of adverse events such as dry mouth, constipation, drowsiness and postural hypotension was low. Complaints concerning the upper intestinal tract, such as epigastric distress, were predominant in the FLU group. MIL treatment is therefore preferred.

L67 ANSWER 10 OF 35 DRUGU COPYRIGHT 2002 THOMSON DERWENT
ACCESSION NUMBER: 2000-27375 DRUGU T S
TITLE: Milnacipram efficacy in the prevention of recurrent depression: a 12-month placebo-controlled study.
AUTHOR: Rouillon F; Warner B; Pezous N; Bisserbe J C
LOCATION: Creteil, Fr.
SOURCE: Int.Clin.Psychopharmacol. (15, No. 3, 133-40, 2000) 1 Fig. 2 Tab. 45 Ref.
CODEN: ICLPE ISSN: 0268-1315
AVAIL. OF DOC.: Service de Psychiatrie, Hopital Albert Chenevier, 40 Rue de Mesly, 94010 Creteil Cedex, France.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB In a double-blind, placebo-controlled trial in 214 patients with a history of recurrent major depression who had responded to acute milnacipran therapy, long-term p.o. milnacipran treatment decreased recurrence rates. Milnacipran was well tolerated; adverse events were as frequent on placebo as on milnacipran. Adverse events on milnacipran included headache, nausea, anxiety, insomnia, abdominal **pain**, sweating, constipation and vertigo. There was one spontaneous abortion on milnacipran.

L67 ANSWER 11 OF 35 DRUGU COPYRIGHT 2002 THOMSON DERWENT

ACCESSION NUMBER: 1996-45496 DRUGU T S
TITLE: Comparative studies with milnacipran and tricyclic antidepressants in the treatment of patients with major depression: a summary of clinical trial results.
AUTHOR: Kasper S; Pletan Y; Solles A; Tournoux A
CORPORATE SOURCE: Univ.Vienna; Cent.Res.Pierre-Fabre
LOCATION: Waehringer Guertel, Austria; Boulogne, Fr.
SOURCE: Int.Clin.Psychopharmacol. (11, Suppl. 4, 35-39, 1996) 4 Tab. 19 Ref. ISSN: 0268-1315
AVAIL. OF DOC.: Department of General Psychiatry, University of Vienna, A-1090 Vienna, Waehringer Guertel, Austria.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB Milnacipran (MC, Ixel) was as effective as imipramine (IM) and clomipramine (CP) in 7 randomized, double-blind trials totalling 842 patients with major depression. The incidence of adverse events obtained from data from 5732 patients was generally lower with MC than with TCA. Dry mouth, constipation, tremor, increased sweating, somnolence, fatigue, dizziness, orthostatic hypotension, abnormal vision, dysgeusia, malaise and diarrhea occurred more frequently with TCA than with MC, but dysuria occurred more frequently with MC. Other adverse events included nausea, headache, abdominal **pain**, insomnia, vertigo, anxiety, agitation, hot flushes, palpitations, dyspepsia and nervousness.TCA, but not MC, increased the PR interval, QRS duration and corrected QT space. (conference paper).

L67 ANSWER 12 OF 35 DRUGU COPYRIGHT 2002 THOMSON DERWENT
ACCESSION NUMBER: 1991-07594 DRUGU P
TITLE: Antinociceptive Effects of mCCP in Mice After Acute and Chronic Milnacipran or Imipramine Treatment.
AUTHOR: Stenger A; Fabre J; Briley M
LOCATION: Castres, France
SOURCE: Fundam.Clin.Pharmacol. (4, No. 5, 563, 1990) 1 Ref.
CODEN: FCPHEZ ISSN: 0767-3981
AVAIL. OF DOC.: Centre de Recherche Pierre Fabre, 17, avenue Jean Moulin 81100, Castres, France.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB Using the phenylbenzoquinone (PBQ) writhing test, acute p.o. ED50 values were 100 mg/kg for milnacipran and 65 mg/kg for imipramine. The antinociceptive potency of m-chloro-phenylpiperazine (mCCP) was 10 mg/kg p.o. Mice were then administrated the antidepressants acutely (15 mg/kg, p.o.) or in the drinking water for 21 days (mean dose 12-17 mg/kg/day) and mCCP (10 mg/kg, p.o.) given 24 hr after the acute dose or 24 hr after the drug solution was replaced by water. Chronic but not acute imipramine increased mCCP-induced **analgesia**. Milnacipran had no effect, suggesting that 5HT receptor hypersensitivity is not a property common to all antidepressant drugs. (congress abstract).

L67 ANSWER 13 OF 35 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:283758 CAPLUS
DOCUMENT NUMBER: 134:285613
TITLE: Treatment of fatigue, head injury and stroke with a selective noradrenaline reuptake inhibitor combined with phenylalanine or tyrosine
INVENTOR(S): Horrobin, David F.; Loder, Cari
PATENT ASSIGNEE(S): Laxdale Limited, UK
SOURCE: PCT Int. Appl., 17 pp.
CODEN: PIXXD2

Searched by Barb O'Bryen, STIC 308-4291

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001026623	A2	20010419	WO 2000-GB3926	20001012
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
GB 2355191	A1	20010418	GB 1999-24172	19991012

PRIORITY APPLN. INFO.: GB 1999-24172 A 19991012

AB A method of treatment of disorders of neurol. origin and drug formulations for use in the method are disclosed. These conditions comprise fatigue and assocd. syndromes of pain, weakness and depressed mood which are assocd. with **chronic fatigue** syndrome, brain injury and stroke, stress, **fibromyalgia**, and irritable bowel syndrome. The treatment comprises administering to a patient in need thereof a selective inhibitor of noradrenaline reuptake combined with either phenylalanine or tyrosine in the same dosage form or the same pack. The noradrenergic drug may be selected from lofepramine, desipramine or reboxetine. The selective inhibitor may be a combined inhibitor of both noradrenaline and serotonin reuptake such as venlafaxine, duloxetine or **milnacipran**, or an inhibitor of both noradrenaline and dopamine reuptake such as bupropion.

IT **92623-85-3, Milnacipran**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of fatigue, head injury and stroke with a selective noradrenaline reuptake inhibitor combined with phenylalanine or tyrosine)

L67 ANSWER 14 OF 35 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:706961 CAPLUS
DOCUMENT NUMBER: 133:271707
TITLE: Fast-dissolving isotropic expanded microporous composition or structure for pharmaceutical, veterinary, dietetic, food or cosmetic use, and method for obtaining same
INVENTOR(S): Goutay, Eric; Lachamp, Laurence; Frances, Jacques; Bougaret, Joel; Paillard, Bruno
PATENT ASSIGNEE(S): Pierre Fabre Medicament, Fr.
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000057856	A1	20001005	WO 2000-FR803	20000330
W: AU, BR, CA, CN, JP, MX, US, ZA				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
FR 2791569	A1	20001006	FR 1999-4033	19990331
EP 1165052	A1	20020102	EP 2000-915253	20000330

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

PRIORITY APPLN. INFO.: FR 1999-4033 A 19990331
WO 2000-FR803 W 20000330

AB The invention concerns a compn. for pharmaceutical, veterinary, food, dietetic or cosmetic use, comprising 1 wt. % to 50 wt. % of one or several active principle(s), 50 wt. % to 90 wt. % of a carrier comprising one or several polymer(s), optionally one or several diluent(s) and optionally one or several additive(s), in particular flavoring or coloring additives. Said compn. is characterized in that it has a fast-dissolving isotropic microporous expanded structure and the polymers are selected from the group consisting of polymers of plant origin, optionally combined with polymers of animal origin or synthetic polymers, and said carrier is such that the binding polymer(s) are present in the compn. in a proportion not less than 1 % (p/p) and more particularly ranging between 6 % and 98 % (p/p). With respect to the polymer(s), it is a polysaccharide of plant origin, optionally modified by chem. or enzymic process or obtained by chem. or enzymic hydrolysis which is being particularly referred to. A fast-dissolving isotropic expanded microporous compn. contg. phloroglucinol 100, sodium caseinate 40, xylitol 20, and mannitol 400 mg was prepd.

IT **92623-85-3, Milnacipran**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fast-dissolving isotropic expanded microporous compn. or structure for pharmaceutical, veterinary, dietetic, food or cosmetics)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L67 ANSWER 15 OF 35 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2002154765 EMBASE
TITLE: Therapeutic effects of milnacipran, a serotonin and noradrenaline reuptake inhibitor, on post-stroke depression.
AUTHOR: Kimura M.; Kanetani K.; Imai R.; Suzuki H.; Isayama K.; Endo S.
CORPORATE SOURCE: M. Kimura, Department of Neuropsychiatry, Nippon Medical School, 1-1- 5 Sendagi, Bunkyo-ku, Tokyo 113-8602, Japan. mkimura@med.email.ne.jp
SOURCE: International Clinical Psychopharmacology, (2002) 17/3 (121-125).
Refs: 27
ISSN: 0268-1315 CODEN: ICLPE4
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 032 Psychiatry
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Depression is common after stroke. While several reports have been published on the use of antidepressants such as selective serotonin reuptake inhibitors and tricyclics for the treatment of post-stroke depression (PSD), no previous study has examined the use of a selective serotonin and noradrenaline reuptake inhibitor (SNRI) for this condition. The present study investigated the efficacy and safety of milnacipran, a SNRI, for the treatment of PSD. A 6-week open study was conducted in 12 patients (two males and 10 females) aged 53-88 years. All patients were diagnosed with major or minor depressive disorder according to DSM-IV, where onset was subsequent to a cerebral infarction or haemorrhage (stroke). Severity of depression was assessed using the 21-item Hamilton rating scale for depression (HAM-D). The maximum total daily dose of

milnacipran was in the range of 30-75 mg b.i.d. Three patients experienced side-effects, but none of the side-effects were serious. Two patients dropped out of the study. At the end of the study, 58.3% (7/12) of the total patient population and 70% (7/10) of the patients completing the study were in remission (a final HAM-D score of less than 7 and no longer meeting criteria for major or minor depression). These results suggest that milnacipran may be an effective treatment for PSD. .COPYRGT. 2002 Lippincott Williams & Wilkins.

L67 ANSWER 16 OF 35 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2001165752 EMBASE
TITLE: Antidepressant efficacy and tolerability of milnacipran, a dual serotonin and noradrenaline reuptake inhibitor: A comparison with fluvoxamine.
AUTHOR: Clerc G.; Assicot M.; Bouchard J.M.; Cottin M.; Guibert M.; Liegaut D.; Engel P.; May J.P.; Oules J.; Pagot R.; Patris M.F.; Ruimy P.; Sombret A.; Van Amerongen A.P.; Tournoux A.
CORPORATE SOURCE: Dr. A. Tournoux, Departement de Rech. Clinique, Institut de Recherche, Pierre Fabre, 45 Place Abel Gance, 92654 Boulogne, France
SOURCE: International Clinical Psychopharmacology, (2001) 16/3 (145-151).
Refs: 26
ISSN: 0268-1315 CODEN: ICLPE4
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 030 Pharmacology
032 Psychiatry
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The antidepressant efficacy and tolerability of milnacipran, a dual action serotonin-noradrenaline reuptake inhibitor, were compared with those of the selective serotonin reuptake inhibitor, fluvoxamine, in 113 patients with moderate to severe major depression. Treatment with milnacipran, 50 mg b.d. for 6 weeks, produced a significantly greater reduction in Montgomery-Asberg Depression Rating Scale (MADRS) scores than fluvoxamine, 100 mg b.d. (P = 0.007; 65.4% versus 49.9%, respectively); significantly greater decreases were also seen on days 7 (P = 0.04) and 28 (P = 0.03). The response rate (the proportion of patients showing a decrease in MADRS scores of at least 50%) was 78.9% in patients receiving milnacipran, compared with 60.7% in fluvoxamine-treated patients (P= 0.04). Milnacipran also produced greater improvements in 24-item Hamilton Depression Rating Scale scores (P = 0.05). On the Clinical Global Impression Improvement scale, 77.2% of milnacipran-treated patients were rated as considerably or markedly improved, compared with 60.7% of patients receiving fluvoxamine (P = 0.06 chi-squared). Both treatments were well tolerated; the only significant difference between the two groups was a higher incidence of tremor and drowsiness in patients treated with fluvoxamine. It is concluded that milnacipran may offer some advantages over selective serotonin reuptake inhibitors, such as fluvoxamine, in the treatment of moderate to severe major depression. .COPYRGT. 2001 Lippincott Williams & Wilkins.

L67 ANSWER 17 OF 35 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2000212795 EMBASE
TITLE: Milnacipran: An antidepressant with dual selectivity of action on noradrenaline and serotonin uptake.
AUTHOR: Delini-Stula A.
CORPORATE SOURCE: A. Delini-Stula, CNS Med. Research Counselling, Stoberstrasse 36, CH 4055 Basle, Switzerland
SOURCE: Human Psychopharmacology, (2000) 15/4 (255-260).

Refs: 34
ISSN: 0885-6222 CODEN: HUPSEC
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 030 Pharmacology
032 Psychiatry
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Milnacipran is a new antidepressant which possesses potent and doubly selective action in that it inhibits both the re-uptake of serotonin and noradrenaline without any effect on other neurotransmitter systems. The almost equipotent inhibition of serotonin and noradrenaline by milnacipran is functionally reflected in the several-fold and long-lasting increase of the levels of these monoamines in the brain and in antidepressant-like effects in animals. In man, milnacipran distinguishes itself from many other antidepressants by its simple pharmacokinetics. It shows linear dose-concentration relationship over a dose range of 25-200 mg/day. It is rapidly and extensively absorbed and almost completely eliminated after 12 h (t1/2 approx. 8 h). Steady-state plasma levels are reached within 32-48 h after twice daily oral administration. Milnacipran is highly bioavailable (> 85 per cent) and its metabolism does not involve the cytochrome P450 enzyme system. In clinical studies, milnacipran showed antidepressant efficacy similar to that of TCAs and SSRIs and superior to that of placebo. At the optimum dose of 100 mg/day, after 4-8 weeks of treatment, 60-64 per cent of in- or out-patients with major depression improve (.gtoreq. 50 per cent reduction of HAMD and MADRS score) and about 32-39 per cent of them achieve full I-emission (HAMD score .ltoreq. 7). Milnacipran has proved to be a very safe drug with a benign adverse event profile clearly superior to that of TCAs and, to a certain extent, that of SSRIs. Only about 10 per cent of patients experience side-effects and only dysuria occurred more frequently (2 per cent) with milnacipran than with TCAs or SSRIs. Milnacipran appears therefore to be an antidepressant with a very favourable benefit/risk ratio. Copyright (C) 2000 John Wiley and Sons, Ltd.

L67 ANSWER 18 OF 35 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2000137626 EMBASE
TITLE: [New psychotropic drugs: Milnacipran - A fourth generation antidepressant of the first denomination].
NOVA PSYCHOFARMAKA: MILNACIPRAN - ANTIDEPRESIVUM S PRVYM OZNACENIM PRISLUSNOSTI KE CTVRTE GENERACI.
AUTHOR: Svestka J.
CORPORATE SOURCE: Dr. J. Svestka, Psychiatricka Klinika, LF a FN, Jihlavska 20, 639 00 Brno, Czech Republic
SOURCE: Psychiatrie, (2000) 4/1 (46-56).
Refs: 49
ISSN: 1211-7579 CODEN: PCHIF7
COUNTRY: Czech Republic
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 030 Pharmacology
032 Psychiatry
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: Czech
SUMMARY LANGUAGE: English; Czech
AB The mechanism of action of milnacipran consists in the inhibition of noradrenaline and serotonin reuptake. In animal models, the drug exerted an antidepressant effect, did not affect motor action and showed low behavioral toxicity. It is characterized by a high bioavailability, low protein binding, fast, mostly renal elimination, and the biological half-life of 8 hours in average. In clinical trials the antidepressant

effect of milnacipran was greater than that of placebo, comparable with that of tricyclic antidepressants, and higher than that of SSRIs in severe major depressive disorders; its beneficial effect was significant even in depressive patients suffering from anxiety, sleep disorders and suicidal ideations. The tolerability of milnacipran was very good, i.e. significantly better than that of tricyclic antidepressants. The drag did not affect patients' body weight. The miction problems and digoxine administration are the contraindications. Milnacipran has the advantage of minimal risk of pharmacokinetic interactions, which allows the initial co-administration of benzodiazepines.

L67 ANSWER 19 OF 35 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1999256355 EMBASE
TITLE: [Milnacipran new antidepressor clinical tolerability]. TOLERANCE CLINIQUE D'UN NOUVEL ANTIDEPRESSEUR, LE MILNACIPRAN.
AUTHOR: Regina W.; Vandel P.; Vandel S.; Sechter D.; Bizouard P.
CORPORATE SOURCE: W. Regina, Svc. de Psychiatrie/Psychologie Med., CHU Saint-Jacques, 25030 Besancon Cedex, France
SOURCE: Encephale, (1999) 25/3 (252-258).
Refs: 17
ISSN: 0013-7006 CODEN: ENCEAN
COUNTRY: France
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 030 Pharmacology
032 Psychiatry
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: French
SUMMARY LANGUAGE: English; French
AB Milnacipran is a new antidepressant which has been developed for its selective inhibition of both serotonin and noradrenaline reuptake with a good safety and tolerability profile. The efficacy and tolerance profile of this antidepressant have been compared with those of tricyclic and selective serotonin reuptake inhibitor antidepressants (SSRIs) in open-label and placebo-controlled trials. But no data in clinical practice are available. The authors studied the tolerability of milnacipran (100 to 200 mg/d) in 28 depressed inpatients receiving usual comedications during a mean period of 33 days (3 to 107 days). The incidence of adverse events was determined with the help of the Pharmaco-vigilance Center of the Centre Hospitalo-Universitaire (Besancon, France). Among the 28 patients, milnacipran was well tolerated by 18 of them. Side-effects were noted in 10 patients, but they led to withdrawal of the antidepressant in only 2 cases, where dyspnea, palpitations, pollakiuria in a case and headache, nausea, dysuria in the other case occurred. The most frequent adverse event observed was hypotension (n = 6), but in each case it occurred just after the addition of sedative phenothiazines (n = 5) or of a comedication with phenothiazines and valpromide (n = 1). So this side-effect could not be attributed to milnacipran alone. Treatments with heptaminol or theodrenaline and cafedrine were useful. An increase of the cardiac frequency seemed to occur with milnacipran ($p < 0.06$). It was observed in the 5 inpatients for whom this cardiovascular parameter was recorded before and during the milnacipran treatment. In 5 other patients, the cardiac frequency seemed to decrease when milnacipran was stopped for lack of good efficacy or adverse events. Gastrointestinal disturbances were scarce isolated (nausea n = 1), but necessitated a treatment with metopimazine. The milnacipran prescription (100 mg/d) after an other antidepressant treatment had been done without a withdrawal period and without problem, even when the previous antidepressant was a SSRIs with a long half-life and CYP450 inhibitory properties. The authors concluded to the good tolerability of milnacipran in usual clinical practice.

L67 ANSWER 20 OF 35 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 1998324939 EMBASE
TITLE: Milnacipran, a new specific serotonin and noradrenaline reuptake inhibitor.
AUTHOR: Boyer P.; Briley M.
CORPORATE SOURCE: M. Briley, Institut de Recherche Pierre Fabre, Parc Industriel de la Chartreuse, 81100 Castres, France
SOURCE: Drugs of Today, (1998) 34/8 (709-720).
Refs: 50
ISSN: 0025-7656 CODEN: MDACAP
COUNTRY: Spain
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 032 Psychiatry
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Milnacipran is a new antidepressant which inhibits equipotently the reuptake of serotonin and noradrenaline both in vitro and in vivo with no effect on dopamine reuptake. Microdialysis studies have shown increased extracellular levels of both serotonin and noradrenaline after acute administration. Milnacipran is devoid of interactions at any known neurotransmitter receptor. In particular, and unlike tricyclic antidepressants (TCAs), it has no activity at noradrenergic, muscarinic or histaminergic receptors. Contrary to TCAs, chronic administration of milnacipran does not modify beta-adrenoceptor binding or second messenger function. Milnacipran is active on various animal models of depression such as the forced swimming test in the mouse, learned helplessness in the rat and the olfactory bulbectomized rat model. Milnacipran has a high bioavailability, low plasma protein binding, and is largely eliminated in the urine as the parent drug or as a glucuronide. These features suggest that interactions with other drugs given concurrently are unlikely. Studies in patients with liver dysfunction and in the elderly suggest that dose adjustment is not necessary. In patients with renal impairment, decreased elimination of milnacipran is correlated to the degree of renal impairment allowing an easy dosage adjustment. An intermediate half-life of approximately 8 h is compatible with twice-daily administration. Clinical studies comparing milnacipran, placebo and other antidepressants provide evidence of its efficacy in moderate to severe depression in both hospitalized and outpatient settings. Metaanalyses of the original data of controlled trials comparing milnacipran with imipramine or selective serotonin reuptake inhibitors (SSRIs) show that milnacipran provides antidepressant efficacy similar to that of TCAs and significantly superior to that of SSRIs. An analysis of a database of over 3300 patients shows that both the general and cardiovascular tolerability of milnacipran are superior to those of TCAs with notably less cholinergic side effects. The tolerance of milnacipran was comparable to that of SSRIs with a higher incidence of dysuria with milnacipran but a higher frequency of nausea and anxiety with the SSRIs. Milnacipran represents an interesting new therapeutic option in depression, being as well tolerated as the SSRIs but offering clinical efficacy similar to the TCAs.

L67 ANSWER 21 OF 35 EMBASE
ACCESSION NUMBER: 1998333350 EMBASE
TITLE: Milnacipran. A review of its use in depression.
AUTHOR: Spencer C.M.; Wilde M.I.
CORPORATE SOURCE: C.M. Spencer, Adis International Limited, 41 Centorian Drive, Mairangi Bay, Auckland 10, New Zealand. demail@adis.co.nz
SOURCE: Drugs, (1998) 56/3 (405-427).
Refs: 79
ISSN: 0012-6667 CODEN: DRUGAY
COUNTRY: New Zealand
DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 030 Pharmacology
032 Psychiatry
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Milnacipran is a cyclopropane derivative which acts by inhibiting noradrenaline (norepinephrine) and serotonin (5-hydroxytryptamine; 5-HT) reuptake at presynaptic sites; no postsynaptic receptor activity has been demonstrated. It is most commonly administered at a dosage of 50 mg twice daily for the treatment of major depressive disorder. Improvement usually occurs within 2 weeks of treatment initiation, but some patients do respond sooner. Most studies which evaluated milnacipran were of short (4 to 8 weeks) duration and results were not published in full with rigorous peer review. Nonetheless, the drug is significantly more effective than placebo for the treatment of in- or outpatients with moderate to severe major depressive disorder. Limited data suggest that it may prevent relapse and be effective for long term use, although this requires confirmation. Milnacipran 200 mg/day is generally not significantly different from amitriptyline 150 mg/day in terms of onset and efficacy. However, when doses are titrated (not a requirement for milnacipran), milnacipran 50 or 100 mg/day has a slower onset than the tricyclic antidepressant. At a dosage of 100 mg/day for 4 to 12 weeks, milnacipran generally has similar efficacy to imipramine and clomipramine 150 mg/day, although milnacipran 50 to 150 mg/day had a faster onset of activity than imipramine 50 to 150 mg/day in Japanese patients. In a 6-month trial, milnacipran was less effective than clomipramine. Milnacipran 50 or 100 mg twice daily was as effective as fluoxetine 20 mg once daily or fluvoxamine 100 mg twice daily in 4- to 12-week studies. At a dosage of 50 then 100 mg daily it was also as effective as mianserin 30 then 60 mg daily in a 4-week study. However, when administered once daily (in the evening), milnacipran 100 mg/day was not as effective as fluoxetine 20 mg/day after 6 weeks. The drug is generally well tolerated, producing no more adverse events (including anticholinergic events) than placebo, selective serotonin reuptake inhibitors or mianserin and fewer adverse events than tricyclic antidepressants in clinical trials. However, dysuria has been reported in 7% of male patients receiving milnacipran. Conclusions: Data from predominantly short term trials suggest that milnacipran generally has similar efficacy to tricyclic antidepressants and SSRIs. Although further published data are required to confirm its efficacy, good tolerability profile and pharmacokinetic profile which suggests a low potential for drug interactions, milnacipran should be considered a promising agent for the treatment of patients with major depressive disorder.

L67 ANSWER 22 OF 35 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1998106326 EMBASE
TITLE: Double-blind study of the efficacy and safety of milnacipran and imipramine in elderly patients with major depressive episode.
AUTHOR: Tignol J.; Pujol-Domenech J.; Chartres J.P.; Leger J.-M.; Pletan Y.; Tonelli I.; Tournoux A.; Pezous N.
CORPORATE SOURCE: J. Tignol, Universite de Bordeaux II, Hopital Charles Perrens, Service Universitaire de Psychiatrie, 121 Rue de la Bechade, 33076 Bordeaux Cedex, France
SOURCE: Acta Psychiatrica Scandinavica, (1998) 97/2 (157-165). Refs: 32
ISSN: 0001-690X CODEN: APYSA
COUNTRY: Denmark
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 020 Gerontology and Geriatrics
032 Psychiatry
037 Drug Literature Index

038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The novel antidepressant agent milnacipran is a dual and equipotent serotonin and noradrenaline reuptake inhibitor. The aim of this double-blind study was to compare the efficacy and safety of milnacipran (50 mg twice daily) with that of imipramine (50 mg twice daily) in elderly patients with major depressive episode. A total of 219 patients were randomly assigned to 8 weeks of double-blind treatment with either milnacipran or imipramine; 72 patients withdrew from the study. At the end of treatment no significant differences were found between milnacipran and imipramine in antidepressant efficacy. A significantly greater number of side-effects, particularly anticholinergic effects, was observed in the imipramine group. Milnacipran may be preferable to imipramine in elderly depressed patients, as it provides the same antidepressant activity as imipramine with a lower incidence of side-effects, and does not impair cognitive ability.

L67 ANSWER 23 OF 35 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1998129084 EMBASE
TITLE: Milnacipran. New preparation.
SOURCE: Prescrire International, (1998) 7/34 (51-53).
Refs: 15
ISSN: 1167-7422 CODEN: PRINFU
COUNTRY: France
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 030 Pharmacology
032 Psychiatry
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Several placebo-controlled trials have shown that milnacipran, 100 mg/day in two doses, is an effective antidepressant in both the ambulatory and hospital settings. Comparative trials against tricyclic antidepressants (imipramine and clomipramine) failed to show that milnacipran was any more effective. Milnacipran has not been compared with specific or non specific MAOI antidepressants. As regards non tricyclic-non MAOI antidepressants, milnacipran has been compared only to two specific serotonin reuptake inhibitors, fluvoxamine and fluoxetine. The trials cannot convince us of a difference in efficacy between the two types of treatment. The claimed superiority of milnacipran over serotonin reuptake inhibitors is not based on firm evidence of better efficacy or fewer adverse effects. The overall tolerability of milnacipran is similar to that of fluoxetine and fluvoxamine. Relative to the tricyclic antidepressants, milnacipran has fewer atropinic effects (sedation and sweating). In contrast, it causes more dysuria, and cannot, therefore, replace tricyclics in elderly men with prostate disorders. Tricyclics remain the preferred first-line antidepressant drugs. When they are contraindicated or poorly tolerated, many other antidepressants with well-documented risk-benefit ratios are available.

L67 ANSWER 24 OF 35 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 97276999 EMBASE
DOCUMENT NUMBER: 1997276999
TITLE: The place of milnacipran in the treatment of depression.
AUTHOR: Kasper S.
CORPORATE SOURCE: S. Kasper, Department of General Psychiatry, University of Vienna, Wahringer Gurtel 18-20, A-1090 Vienna, Austria
SOURCE: Human Psychopharmacology, (1997) 12/SUPPL. 3 (S135-S141).
Refs: 32
ISSN: 0885-6222 CODEN: HUPSEC
COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 008 Neurology and Neurosurgery
032 Psychiatry
036 Health Policy, Economics and Management
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Modern community-based studies have revealed high prevalence rates for major depression in adults. Despite this high prevalence, many depressed individuals do not seek treatment and only a minority of those that do are prescribed antidepressants. This paper considers the role of antidepressants, especially of milnacipran in the treatment of major depression. Milnacipran inhibits the reuptake of serotonin and noradrenaline (SNRI) in a selective manner without affecting various postsynaptic receptor sites; this results in a favourable tolerability profile of the drug. Minimising adverse events is important to enhance patient compliance and facilitate the administration of therapeutic doses of antidepressants. Data from placebo-controlled trials and the results of comparator studies involving TCAs and SSRIs have confirmed that milnacipran is an effective and well tolerated antidepressant, particularly useful in patients with severe depression. A recent pharmacoeconomic study has confirmed that milnacipran is a cost effective alternative to TCAs and SSRIs in the treatment of severe depression.

L67 ANSWER 25 OF 35 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 97203862 EMBASE
DOCUMENT NUMBER: 1997203862
TITLE: Milnacipran, a new serotonin and noradrenaline reuptake inhibitor: An overview of its antidepressant activity and clinical tolerability.
AUTHOR: Puech A.; Montgomery S.A.; Prost J.F.; Solles A.; Briley M.
CORPORATE SOURCE: M. Briley, Centre de Recherche Pierre Fabre, 81100 Castres, France
SOURCE: International Clinical Psychopharmacology, (1997) 12/2 (99-108).
Refs: 26
ISSN: 0268-1315 CODEN: ICLPE4
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 032 Psychiatry
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Milnacipran (Ixel.RTM.) is a new antidepressant with essentially equal potency for inhibiting the reuptake of both serotonin and noradrenaline, with no affinity for any neurotransmitter receptor studied. A review of the studies comparing milnacipran, placebo and active comparator antidepressants provides clear-cut evidence of its efficacy in both severe and moderate depression in hospitalized and community settings. Meta-analyses of the original data of controlled trials involving 1032 patients, comparing milnacipran with imipramine or selective serotonin reuptake inhibitors (SSRIs), show that milnacipran provides antidepressant efficacy similar to that of imipramine and significantly superior to that of the SSRIs. An analysis of a database of over 3300 patients shows that both the general and cardiovascular tolerability of milnacipran are superior to those of the tricyclic antidepressants (TCAs) with fewer cholinergic side-effects. The tolerability of milnacipran was comparable to that of the SSRIs, with a higher incidence of dysuria with milnacipran, and a higher frequency of nausea and anxiety with the SSRIs. Milnacipran is a new therapeutic option in depression, which offers a clinical efficacy in the range of the TCAs combined with a tolerability equivalent

to that of the SSRIs.

L67 ANSWER 26 OF 35 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 93076067 EMBASE
DOCUMENT NUMBER: 1993076067
TITLE: Milnacipran hydrochloride.
SOURCE: Drugs of the Future, (1993) 18/1 (83-84).
ISSN: 0377-8282 CODEN: DRFUD4
COUNTRY: Spain
DOCUMENT TYPE: Journal; (Short Survey)
FILE SEGMENT: 008 Neurology and Neurosurgery
032 Psychiatry
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English

L67 ANSWER 27 OF 35 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 87089373 EMBASE
DOCUMENT NUMBER: 1987089373
TITLE: An early clinical trial of midalcipran, 1-phenyl-1-diethyl aminocarbonyl 2-aminomethyl cyclopropane (Z) hydrochloride, a potential fourth generation antidepressant.
AUTHOR: Serre C.; Clerc G.; Escandé M.; et al.
CORPORATE SOURCE: Department Recherche Clinique, Centre de Recherche Pierre Fabre, 81106 Castres, France
SOURCE: Current Therapeutic Research - Clinical and Experimental, (1986) 39/1 (156-164).
CODEN: CTCEA
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
038 Adverse Reactions Titles
030 Pharmacology
032 Psychiatry
LANGUAGE: English
AB Midalcipran, (F 2207) (1-phenyl-1-diethyl aminocarbonyl 2-aminomethyl cyclopropane (Z) hydrochloride), is an original cyclopropanic antidepressant compound which exhibits an equal potency for the inhibition of both the uptake of noradrenalin and serotonin and characterized by a total absence of post-synaptic effects. This potential fourth-generation antidepressant was evaluated for its antidepressant effect and tolerance in a preliminary open phase II study. Of 27 in-patients suffering from major depressive disorders, 25 were treated orally from 14 to 28 days with 100 mg to 200 mg/day. Excellent or good results were obtained in 68%, and moderate in 12%. Eight per cent were estimated doubtful and 12% bad, (3 cases) amongst whom 2 concerned patients who were non-responders to ECT. Hamilton Depression Scale ratings fell from an initial mean (.+-. SEM) of 26.4 (.+-. 1) to 8.1 (.+-. 1.3) after four weeks and MADRS from 39.2 (.+-. 1.5) to 11.1 (.+-. 2.5). No anticholinergic or significant cardio-vascular effects were observed, and the most troublesome side effects were vomiting in 1 patient. Worsening of difficulties in falling asleep appeared in 29% of cases, all but one of which came from the same centre. Increasing the daily dose from 100 mg to 200 mg appeared to confer no special benefit, which suggests that 100 mg should be chosen for further controlled studies. From the study, it appears that midalcipran, one of the first fourth-generation antidepressants, possesses an interesting clinical profile. If confirmed, this profile suggests that midalcipran may represent a significant advance in the treatment of affective disorders.

L67 ANSWER 28 OF 35 ADISALERTS COPYRIGHT 2002 (ADIS)
ACCESSION NUMBER: 2000:11152 ADISALERTS
DOCUMENT NUMBER: 800826902

TITLE: New composition for treating disorder of central nervous system comprises norepinephrine reuptake inhibitor and antimuscarinic agent.
DERWENT CLASS: B05
INVENTOR(S): JORN, D; ROGOSKY, K
PATENT ASSIGNEE(S): (PHAA) PHARMACIA & UPJOHN CO; (JORN-I) JORN D; (ROGO-I) ROGOSKY K
COUNTRY COUNT: 94
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001062236	A2	20010830	(200164)*	EN	21
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2001038028	A	20010903	(200202)		
US 2002010216	A1	20020124	(200210)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001062236	A2	WO 2001-US3698	20010123
AU 2001038028	A	AU 2001-38028	20010223
US 2002010216	A1 Provisional	US 2000-184790P	20000224
		US 2001-792718	20010223

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2001038028	A Based on	WO 200162236

PRIORITY APPLN. INFO: US 2000-184790P 20000224; US 2001-792718 20010223

AB WO 200162236 A UPAB: 20011105
NOVELTY - A composition comprises .
(a) at least one norepinephrine reuptake inhibitor; and
(b) at least one antimuscarinic agent.
ACTIVITY - Uropathic; Anorectic; Antidepressant; Neuroleptic; Tranquilizer; Nootropic; Antiemetic; Hypotensive; Antimigraine; **Analgesic**; Endocrine; Anabolic; .
MECHANISM OF ACTION - None given.
USE - The composition is useful for treating incontinence e.g. stress incontinence and/or genuine stress incontinence; disease or disorder of the central nervous system selected from obesity, depression, schizophrenia, stress related disease such as general anxiety disorder, panic disorder, phobia, obsessive compulsive disorder, post-traumatic-stress syndrome, immune system depression, a stress induced problem with the urinary, gastrointestinal or cardiovascular system, neurodegenerative disorder, autism, chemotherapy-induced vomiting, hypertension, migraine headaches, cluster headaches, sexual dysfunction in mammal, additive disorder and withdrawal syndrome, an adjustment disorder, an age-associated learning and mental disorder, anorexia nervosa, apathy, an attention-deficit disorder due to general medical conditions, attention-deficit hyperactivity disorder, bipolar disorder, bulimia nervosa, **chronic fatigue** syndrome, conduct disorder, cyclothymic disorder, dysthymic disorder, **fibromyalgia** and other somatoform disorders, generalized anxiety, an inhalation disorder, an

TITLE: **Milnacipran** efficacy in the prevention of recurrent depression: a 12-month placebo-controlled study
ADIS TITLE: **Milnacipran**: therapeutic use.; Depression; Prevention of recurrence
AUTHOR: Rouillon F; Warner B; Pezous N; Bisserbe J C; Milnacipran Recurrence Prevention Study Group
CORPORATE SOURCE: Hopital Albert Chenevier, Creteil, France
SOURCE: International Clinical Psychopharmacology Int Clin Psychopharmacol 15: 133 140, May 2000. (May 1, 2000)
DOCUMENT TYPE: (Clinical study); Abstract
REFERENCE: Affective Disorders (Summary): Alert no. 6, 2000
FILE SEGMENT: Summary
LANGUAGE: English
WORD COUNT: 749

L67 ANSWER 29 OF 35 CBNB COPYRIGHT 2002 EI
ACCESSION NUMBER: 17(34):45242 CBNB
TITLE: Cypress Bioscience in-licenses bioMerieux Pierre Fabre drug for development in **fibromyalgia** treatment.
SOURCE: (1 Aug 2001), 3 pp, (200-899 words)
Availability: Cypress BioScience Inc, Tel: 858 452 2323
DOCUMENT TYPE: Press Release
LANGUAGE: English
AB Cypress Bioscience has signed a license deal with Pierre Fabre Medicament, the drugs division of bioMerieux Pierre Fabre, to develop and sell any product with the compound **milnacipran**, as an active ingredient, for the treatment of **fibromyalgia** syndrome (FMS) and related chronic **pain** syndromes in the US and Canada. The agreement also gives Cypress an option to expand the license to include other indications. Cypress expects to begin trials designed to test the clinical efficiency of **milnacipran** in FMS early next year. Cypress wants to become the leading commercial entity focused on the treatment of FMS and to develop the first approved drug for this condition. Cypress will pay Pierre Fabre an upfront payment to license the compound and milestone payments.

L67 ANSWER 30 OF 35 CIN COPYRIGHT 2002 ACS
AB Cypress Bioscience Inc. (CYPB), San Diego, Calif., will begin in the first half of 2002 a U.S. Phase II trial of **milnacipran** to treat **fibromyalgia** syndrome (FMS) in 200 patients. The product, which is partnered with bioMerieux Pierre Fabre (Paris, France), is marketed as an antidepressant in Europe, South America and Asia.

L67 ANSWER 31 OF 35 CIN COPYRIGHT 2002 ACS
AB Cypress Bioscience Inc. (CYPB), San Diego, Calif., received an exclusive license from bioMerieux Pierre Fabre's (Paris, France), division, PierreFabre Medicament, to develop and market any product containing the active ingredient **milnacipran**, a modulator of the neurotransmitters serotonin and noradrenaline, to treat **fibromyalgia** syndrome (FMS) and related chronic **pain** syndromes. CYPB also received an option to expand the license to include other indications. Fabre will receive an upfront payment, is eligible for milestones and royalties and retains the right to sell FMS products developed by CYPB outside North America, for which CYPB will receive royalties. **Milnacipran** is marketed as an antidepressant in Europe, South America and Asia. CYPB plans to begin clinical trials in FMS early next year.

L67 ANSWER 32 OF 35 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2001-570594 [64] WPIDS
DOC. NO. CPI: C2001-169592

intoxication disorder, a movement disorder, oppositional defiant disorder, **pain** disorder, peripheral neuropathy, post-traumatic stress disorder, premenstrual dysphoric disorder, psychotic disorder, seasonal affective disorder, sleep disorder, specific developmental disorder and selective serotonin reuptake inhibition (SSRI) poop out syndrome (all claimed).

ADVANTAGE - The composition provides rapid relief with minimal amount of deleterious side effects.

Dwg.0/0

L67 ANSWER 33 OF 35 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2001-293343 [31] WPIDS
DOC. NO. CPI: C2001-089996
TITLE: Formulations for treating fatigue, e.g. due to **chronic fatigue** syndrome, fibromylagia or brain infections, comprise selective noradrenaline reuptake inhibitor in combination with phenylalanine or tyrosine.
DERWENT CLASS: B05
INVENTOR(S): CARI, L; HORROBIN, D F; LODER, C
PATENT ASSIGNEE(S): (LAXD-N) LAXDALE LTD
COUNTRY COUNT: 93
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
GB 2355191	A	20010418	(200131)*		13
WO 2001026623	A2	20010419	(200131)	EN	

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW

AU 2000079328 A 20010423 (200147)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
GB 2355191	A	GB 1999-24172	19991012
WO 2001026623	A2	WO 2000-GB3926	20001012
AU 2000079328	A	AU 2000-79328	20001012

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2000079328	A Based on	WO 200126623

PRIORITY APPLN. INFO: GB 1999-24172 19991012

AB GB 2355191 A UPAB: 20010620

NOVELTY - Formulations for treating fatigue comprise a selective noradrenaline reuptake inhibitor (I) in combination with either phenylalanine or tyrosine in the same dosage forms or the same packs.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a unit dosage form containing 50-100 mg lofepramine and 100-1000 mg phenylalanine or tyrosine;

(2) a unit dosage form containing 50-100 mg desipramine and 100-1000 mg phenylalanine or tyrosine; and

(3) a unit dosage form containing 2-5 mg reboxetine and 100-1000 mg phenylalanine or tyrosine.

USE - The formulations are useful for treating **fatigue** due to **chronic fatigue** syndrome, fibromylagia or brain infections (including viral, prion and bacterial infections), fatigue due to brain injury or stroke, and conditions associated with **chronic fatigue** or **fibromyalgia**, especially irritable bowel syndrome, and also for assisting in the recovery of normal brain function after brain injury or stroke, for treating chronic stress, and for treating depression, especially chronic depression or depression after brain injury, brain infection or stroke. In a trial on 138 multiple sclerosis patients, in which half the patients received lofepramine (70 mg) and l-phenylalanine (500 mg) twice a day and the other half received placebos, and in which the patients were assessed on the Gulick scale (Nursing Res., 38, 147, 1989) at baseline, 2 weeks, 3 months and 6 months, the increase in Gulick score was 10.63 for the treated patients and 3.68 for the placebo patients. The improvement in fatigue among the treated patients was 21% over baseline.
Dwg.0/0

L67 ANSWER 34 OF 35 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2001-345718 [37] WPIDS
DOC. NO. CPI: C2001-107126
TITLE: Treating abnormal circadian rhythm or depression comprises administering a corticotropin-releasing factor (CRF) antagonist optionally combined with a second compound having a delayed onset of action compared to the CRF antagonist.
DERWENT CLASS: B02
INVENTOR(S): CHEN, Y L
PATENT ASSIGNEE(S): (PFIZ) PFIZER PROD INC
COUNTRY COUNT: 31
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 1082960	A2	20010314	(200137)*	EN	29
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
AU 2000053644	A	20010301	(200137)		
CA 2316662	A1	20010227	(200137)	EN	
JP 2001097889	A	20010410	(200137)		35
HU 2000003386	A2	20010730	(200157)		
KR 2001050223	A	20010615	(200172)		
ZA 2000004362	A	20020327	(200230)		63

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 1082960	A2	EP 2000-307074	20000818
AU 2000053644	A	AU 2000-53644	20000825
CA 2316662	A1	CA 2000-2316662	20000825
JP 2001097889	A	JP 2000-251836	20000823
HU 2000003386	A2	HU 2000-3386	20000824
KR 2001050223	A	KR 2000-49907	20000826
ZA 2000004362	A	ZA 2000-4362	20000824

PRIORITY APPLN. INFO: US 1999-151183P 19990827
AB EP 1082960 A UPAB: 20010704
NOVELTY - Treating (i) disorders that can be treated by altering circadian rhythm and (ii) depression comprises administering a corticotropin-releasing factor (CRF) antagonist and in case (ii) also administering a second compound for treating depression which has an onset of action that

is delayed with respect to that of the CRF antagonist.

DETAILED DESCRIPTION - Treating (i) disorders that can be treated by altering circadian rhythm and (ii) depression comprises administering a corticotropin-releasing factor (CRF) antagonist and in case (ii) also administering a second compound for treating depression which has an onset of action that is delayed with respect to that of the CRF antagonist.

INDEPENDENT CLAIMS are also included for the following:

(1) a pharmaceutical composition for treating abnormal circadian rhythm or depression, comprising a CRF antagonist, where depression is further treated with a second compound for treating depression, where the second compound has an onset of action that is delayed with respect to that of the CRF antagonist;

(2) a method for treating or preventing a cardiovascular disease, comprising administering a CRF antagonist in combination with a non-CRF antagonist compound;

(3) a method for treating migraine or non-migraine headache, comprising administering a CRF antagonist in combination with a non-CRF antagonist compound; and

(4) a method for treating emesis, comprising administering a CRF antagonist in combination with a non-CRF antagonist compound.

ACTIVITY - Cardiant; antidepressant; anti-insomnia; anti-sleep disorder; antiemetic; vasotropic; antimigraine; analeptic.

No supporting biological data is included.

MECHANISM OF ACTION - The active compounds are corticotropin-releasing factor (CRF) antagonists, serotonin reuptake inhibitors, norepinephrine reuptake inhibitors, noradrenaline reuptake inhibitors, alpha 2-adrenoreceptor agonists, 5HT(1A) inhibitors, monoamine oxidase type A inhibitors, serotonin receptor modulators, serotonin mimics and non-CRF antagonists such as tachykinin antagonists including Nk1 antagonists and 5-HT3 antagonists.

USE - The method is useful for treating depression and for treating time zone change syndrome, seasonal affective disorder, irregular sleep-wake pattern, delayed sleep phase syndrome, advanced sleep phase syndrome, non-24 hour sleep wake disorder, light-induced clock resetting, REM sleep disorder, hypersomnia, parasomnia, narcolepsy, nocturnal enuresis, restless legs syndrome, sleep apnea, dysthymia and abnormal circadian rhythm associated with chronic administration and withdrawal of antidepressant agents. The methods are also useful for treating or preventing cardiovascular disease, migraine or non-migraine headache and emesis induced by pregnancy, vestibular disorder, post-operative sickness, gastrointestinal obstruction, reduced gastrointestinal motility, visceral **pain**, migraine, change in intercranial pressure, chemotherapy, radiation, toxins and opioid **analgesics** (claimed).

Dwg.0/0

L67 ANSWER 35 OF 35 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 1997-414968 [38] WPIDS
DOC. NO. CPI: C1997-132788
TITLE: New 4-substituted piperidin-1-yl carbonyl and piperazin-1-yl carbonyl derivatives - useful in treatment of e.g. depression, obsessive compulsive disorders, anxiety and panic attacks.
DERWENT CLASS: B02 B03
INVENTOR(S): CHOPIN, P; HALAZY, S; JORAND, L C; MARIEN, M; PAUWELS, P; JORAND-LEBRUN, C
PATENT ASSIGNEE(S): (FABR) FABRE MEDICAMENT SA PIERRE
COUNTRY COUNT: 27
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9728141	A1	19970807	(199738)*	FR	132

RW: AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE

W: AU BR CA CN JP KR MX NZ US
FR 2744449 A1 19970808 (199739) 77
AU 9716074 A 19970822 (199801)
EP 880512 A1 19981202 (199901) FR
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
BR 9707251 A 19990406 (199920)
CN 1214047 A 19990414 (199933)
MX 9806255 A1 19981101 (200022)
JP 2000505795 W 20000516 (200032) 115

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9728141	A1	WO 1997-FR203	19970203
FR 2744449	A1	FR 1996-1273	19960202
AU 9716074	A	AU 1997-16074	19970203
		WO 1997-FR203	19970203
EP 880512	A1	EP 1997-902427	19970203
		WO 1997-FR203	19970203
BR 9707251	A	BR 1997-7251	19970203
		WO 1997-FR203	19970203
CN 1214047	A	CN 1997-193122	19970203
MX 9806255	A1	MX 1998-6255	19980803
JP 2000505795	W	JP 1997-527377	19970203
		WO 1997-FR203	19970203

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9716074	A	Based on	WO 9728141
EP 880512	A1	Based on	WO 9728141
BR 9707251	A	Based on	WO 9728141
JP 2000505795	W	Based on	WO 9728141

PRIORITY APPLN. INFO: FR 1996-1273 19960202

AB WO 9728141 A UPAB: 19971006
4-Substituted piperidin-1-yl carbonyl and piperazin-1-yl carbonyl derivatives of formula (I) are new. R1 = H or 1-6C alkyl; Z2 = O, NH, CH2O or CH2NH; R2,R3 = H, alkyl, alkoxy, thioether, nitrile, CF3 or halo; or R2+R3 when adjacent = 5-6 membered ring; X-Y = NCH2, CHCH2, C=CH, N or NCH2CH2; Z1 = e.g. (CH2)n, (CH2)nCO, CO, SO2(CH2)n, O(CH2)n, O(CH2)nCO, OCO, NH(CH2)n, NHSO2(CH2)n, CH=CHCO, -C triple bond C-O-, (CH2)nSO2 or O(CH2)nSO2; provided that when X-Y = CHCH2, then Z1 may also be e.g. O, NH, CONH, SO2NH, OCONH, NHCOO, NH(CH2)nSO2NH, NH(CH2)nCONH, NHCO(CH2)nNH or NHSO2(CH2)nNH; n = 1-6; and when X-Y = CHCH2 or C=CH, Z1 may also be CH=CH or C=C; Ar1 = Ph, naphthyl or pyridyl (all optionally substituted) or they are substituted on 2 adjacent carbons to form a ring; or Ar1-Z1 = tetrahydronaphthyl linked to X by a saturated carbon; R4 = 1-6C alkyl; and R4' = H or 1-6C alkyl.

USE - (I) are used in the treatment or prevention of depression, obsessive compulsive disorders, anxiety, panic attacks, schizophrenia, aggression, bulimia, alcoholism, **pain**, neurodegenerative disorders such as Parkinson's or Alzheimer's disease and cancer. (I) may be used in combination with at least one antidepressant, especially **Milnacipran** and/or a 5HT-1a antagonist (all claimed). (I) are powerful and selective 5HT-1D alpha and beta receptor antagonists. Administration is preferably oral and in a daily dosage of 0.001-1 (preferably 0.005-0.25) g.
Dwg.0/0

FILE 'HOME' ENTERED AT 14:03:10 ON 31 MAY 2002

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199402
ENTRY DATE: Entered STN: 19940215
Last Updated on STN: 19940215
Entered Medline: 19940202

AB OBJECTIVE: This article reviews the literature on the general health, health care utilization, prevalence, medical comorbidity, and treatment of dysthymia in medical settings. METHOD: The literature was searched by using MEDLINE and by reviewing the bibliographies of recent publications. Studies were selected that included health data on patients with dysthymia or chronic depression according to DSM-III, DSM-III-R, ICD-9, or RDC criteria, or patients who were described as having persistent depressive symptoms. RESULTS: This review shows that dysthymic patients are at increased risk for poor general health and frequently use medical services. Compared to the general population, dysthymia is more prevalent in primary care and among patients with various medical and neurological conditions, sleep disorders, chronic fatigue, hypothyroidism, and somatoform disorders. Pharmacotherapy is effective, but has not been well studied. Non-tricyclic antidepressants might be especially useful. Psychotherapy studies are virtually non-existent. CONCLUSIONS: Although dysthymia is considered a minor depressive condition, these findings show that it is a significant public health problem, comparable to major depression. Recent efforts to improve the recognition and treatment of major depression in medical settings, therefore, should be extended to include the entire spectrum of depressive disorders. Future studies should investigate the type and pattern of medical comorbidity and health care utilization, different antidepressant and psychosocial therapies, and the clinical and biological correlates of treatment response in different chronic depressive subtypes in medical settings and compare them to major depressive and subsyndromal depressive conditions.

L90 ANSWER 6 OF 49 MEDLINE
ACCESSION NUMBER: 93155004 MEDLINE
DOCUMENT NUMBER: 93155004 PubMed ID: 8428892
TITLE: Psychotropic treatment of chronic fatigue syndrome and related disorders.
AUTHOR: Goodnick P J; Sandoval R
CORPORATE SOURCE: Department of Psychiatry, University of Miami, FL 33136.
SOURCE: JOURNAL OF CLINICAL PSYCHIATRY, (1993 Jan) 54 (1) 13-20.
Ref: 46
Journal code: 7801243. ISSN: 0160-6689.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199303
ENTRY DATE: Entered STN: 19930326
Last Updated on STN: 19930326
Entered Medline: 19930305

AB BACKGROUND: Chronic fatigue syndrome (CFS) and fibromyalgia frequently are associated with symptoms of major depression. For this reason, antidepressants have been used in treatment of these disorders; however, little direction has been provided into this application in psychopharmacology. METHOD: First, nine studies were reviewed regarding the relationship of the symptoms of fatigue and depression. Next, 23 reports (12 double-blind studies, 7 open studies, and 4 case reports) were reviewed for the effectiveness of therapy as assessed by global response

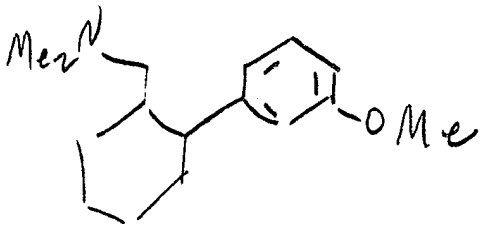
and improvement of both depression and pain. Studies were differentiated by type of controls, as well as by alleged mechanism of action of the pharmacologic agent. RESULTS: Disturbances in brain neurochemistry shared by CFS and major depression may serve as a basis for the effectiveness of some antidepressants in CFS. Response to some antidepressants in patients with CFS or fibromyalgia may occur at doses lower than those used in major depression, e.g., amitriptyline 25-75 mg/day. We further found that the more serotonergic treatments (e.g., clomipramine) were more successful in alleviating pain than depression, whereas catecholaminergic agents (e.g., maprotiline, bupropion) seemed particularly effective for symptoms of associated depression. CONCLUSION: To maximize response of the physiologic and psychological consequences of the disorder, more investigation is needed to replicate the apparent findings that relate the neurochemical impairment underlying CFS and fibromyalgia to the type of antidepressant mechanism.

L90 ANSWER 7 OF 49 MEDLINE
ACCESSION NUMBER: 93074499 MEDLINE
DOCUMENT NUMBER: 93074499 PubMed ID: 1842193
TITLE: Polysomnography in idiopathic muscle pain syndrome (fibrositis).
AUTHOR: Silva A B; Bertorini T E; Lemmi H
CORPORATE SOURCE: Sleep Disorders Center, Baptist Memorial Hospital, Memphis, TN.
SOURCE: ARQUIVOS DE NEURO-PSIQUIATRIA, (1991 Dec) 49 (4) 437-41. Journal code: 0125444. ISSN: 0004-282X.
PUB. COUNTRY: Brazil
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199212
ENTRY DATE: Entered STN: 19930122
Last Updated on STN: 19930122
Entered Medline: 19921201

AB Muscle pain occurs in various neuromuscular disorders with characteristic physiological or biochemical abnormalities. There is, however, a group of patients in whom there is no clear physiological or structural basis for their pains. This syndrome has been called fibrositis or fibromyalgia. Sleep abnormalities have been reported in some of these patients, but have not been confirmed by others. We studied 8 patients with this disorder and found sleep abnormalities that were characterized by nocturnal myoclonus, alpha-delta sleep, and abnormalities compatible with depression. Polysomnography was, therefore, instrumental in helping direct the treatment of these patients. Therapeutic approaches aimed to correct the specific disorders were effective in improving the pain symptoms.

L90 ANSWER 8 OF 49 MEDLINE
ACCESSION NUMBER: 92002557 MEDLINE
DOCUMENT NUMBER: 92002557 PubMed ID: 1912132
TITLE: Nortriptyline in chronic fatigue syndrome: a double blind, placebo-controlled single case study.
AUTHOR: Gracious B; Wisner K L
CORPORATE SOURCE: Department of Psychiatry, University of Pittsburgh School of Medicine, PA 15213.
SOURCE: BIOLOGICAL PSYCHIATRY, (1991 Aug 15) 30 (4) 405-8. Journal code: 0213264. ISSN: 0006-3223.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
(CONTROLLED CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199110

L25 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2002 ACS
AN 1998:301044 CAPLUS
DN 128:303998
TI Tramadol in the fibromyalgia syndrome. A controlled clinical trial versus placebo
AU Biasi, Giovanni; Manca, S.; Manganelli, S.; Marcolongo, R.
CS Inst. Rheumatology, Policlinico Le Scotte, University Siena, Siena, I-53100, Italy
SO International Journal of Clinical Pharmacology Research (1998), 18(1), 13-19
CODEN: CPHRDE; ISSN: 0251-1649
PB Bioscience Ediprint Inc.
DT Journal
LA English
AB The analgesic action of tramadol was assessed compared with placebo in patients suffering from fibromyalgia syndrome. Patients were randomly allocated to either tramadol (100 mg ampoule in 100 mL given i.v.) or placebo for a single dose treatment. Then patients crossed over to the other drug for a further single treatment. There was a wash-out period of 1 wk. Nine patients completed the study, while in 3 cases (2 tramadol, 1 placebo) the study was discontinued due to the onset of side effects. The assessment of efficacy, carried out at the baseline and 15 min and 2 h after administration of each dose, involved the use of a visual analog scale (VAS 100 mm) for spontaneous pain and pressure dolorimetry (kg/cm2) at 12 symptomatic tender points and 9 control tender points for fibromyalgic pain. During the 1st treatment cycle effective control of spontaneous pain was achieved with tramadol, which detd. a redn. of 20.6% while with the placebo spontaneous pain increased by 19.8%. Analgesics tramadol fibromyalgia syndrome.



FILE

ANSWER 1 OF 1 CAPLUS COPYRIGHT 2002 ACS

AN 2000:688075 CAPLUS

DN 133:232864

TI Treatment of neuropathic pain or fibromyalgia with sibutramine and N-demethyl derivatives thereof

IN Mendel, Carl M.; Seaton, Timothy B.; Weinstein, Steve P.

PA Knoll Pharmaceutical Company, USA

SO PCT Int. Appl., 17 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000056318	A1	20000928	WO 2000-US7204	20000317

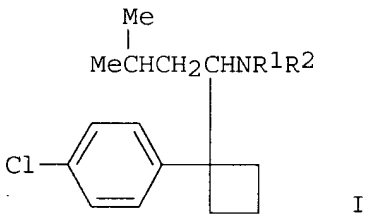
W: AT, AU, BG, BR, CA, CN, CZ, DE, DK, ES, FI, GB, HR, HU, ID, IL, IN, IS, JP, KR, LT, LU, LV, MX, NO, NZ, PL, PT, RO, RU, SE, SG, SI, SK, TR, UA, ZA

RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

PRAI US 1999-125113P P 19990319

OS MARPAT 133:232864

GI



I

AB Compds. I (R1, R2 = H, Me) or a pharmaceutically acceptable salt thereof (e.g. N,N,-dimethyl-1-[1-(4-chlorophenyl)cyclobutyl]-3-methylbutylamine-HCl, optionally in the form of its monohydrate) are used for treating fibromyalgia or neuropathic pain, e.g. pain assocd. with diabetes mellitus, shingles, nerve injury and varied peripheral neuropathies.

RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

PDR® entry for

NEURONTIN® (Parke-Davis)
(gabapentin) capsules
NEURONTIN®
(gabapentin) tablets
NEURONTIN®
(gabapentin) oral solution

Description

DESCRIPTION

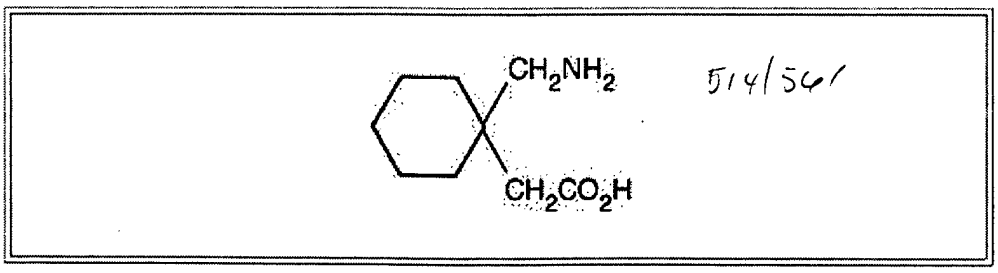
Neurontin® (gabapentin) capsules, Neurontin® (gabapentin) tablets, and Neurontin® (gabapentin) oral solution are supplied as imprinted hard shell capsules containing 100 mg, 300 mg, and 400 mg of gabapentin, elliptical film-coated tablets containing 600 mg and 800 mg of gabapentin or an oral solution containing 250 mg/5 mL of gabapentin.

The inactive ingredients for the capsules are lactose, cornstarch, and talc. The 100 mg capsule shell contains gelatin and titanium dioxide. The 300 mg capsule shell contains gelatin, titanium dioxide, and yellow iron oxide. The 400 mg capsule shell contains gelatin, red iron oxide, titanium dioxide, and yellow iron oxide. The imprinting ink contains FD&C Blue No. 2 and titanium dioxide.

The inactive ingredients for the tablets are poloxamer 407, copolyvidonum, cornstarch, magnesium stearate, hydroxypropyl cellulose, talc, candelilla wax and purified water. The imprinting ink for the 600 mg tablets contains synthetic black iron oxide, pharmaceutical shellac, pharmaceutical glaze, propylene glycol, ammonium hydroxide, isopropyl alcohol and n-butyl alcohol. The imprinting ink for the 800 mg tablets contains synthetic yellow iron oxide, synthetic red iron oxide, hydroxypropyl methylcellulose, propylene glycol, methanol, isopropyl alcohol and deionized water.

The inactive ingredients for the oral solution are glycerin, xylitol, purified water and artificial cool strawberry anise flavor.

Gabapentin is described as 1-(aminomethyl)cyclohexaneacetic acid with an empirical formula of $C_9H_{17}NO_2$ and a molecular weight of 171.24. The molecular structure of gabapentin is:



Gabapentin is a white to off-white crystalline solid. It is freely soluble in water and both basic and acidic aqueous solutions.

PDR® entry for

MIRAPEX® (Pharmacia \& Upjohn)
pramipexole

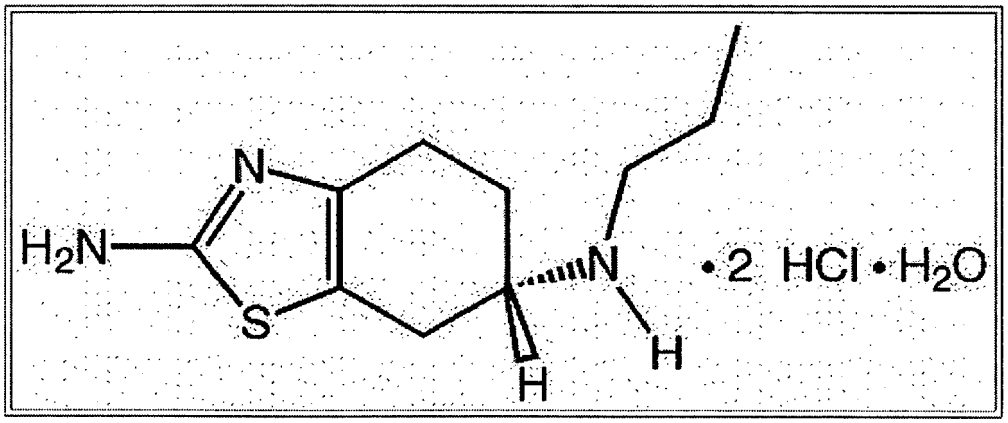
dihydrochloride tablets

Description

DESCRIPTION

MIRAPEX Tablets contain pramipexole, a dopamine agonist indicated for the treatment of the signs and symptoms of idiopathic Parkinson's disease. The chemical name of pramipexole dihydrochloride is (*S*)-2-amino- 4,5,6,7-tetrahydro-6- (propylamino)benzothiazole dihydrochloride monohydrate. Its empirical formula is $C_{10}H_{17}N_3S \cdot 2HCl \cdot H_2O$, and its molecular weight is 302.27.

The structural formula is:



Pramipexole dihydrochloride is a white to off-white powder substance. Melting occurs in the range of 296°C to 301°C, with decomposition. Pramipexole dihydrochloride is more than 20% soluble in water, about 8% in methanol, about 0.5% in ethanol, and practically insoluble in dichloromethane.

MIRAPEX Tablets, for oral administration, contain 0.125 mg, 0.25 mg, 0.5 mg, 1.0 mg, or 1.5 mg of pramipexole dihydrochloride monohydrate. Inactive ingredients consist of mannitol, corn starch, colloidal silicon dioxide, povidone, and magnesium stearate.

(*back to top*)

CLINICAL PHARMACOLOGY

Pramipexole is a nonergot dopamine agonist with high relative in vitro specificity and full intrinsic activity at the D_2 subfamily of dopamine receptors, binding with higher affinity to D_3 than to D_2 or D_4 receptor subtypes. The relevance of D_3 receptor binding in Parkinson's disease is unknown.

PDR® entry for

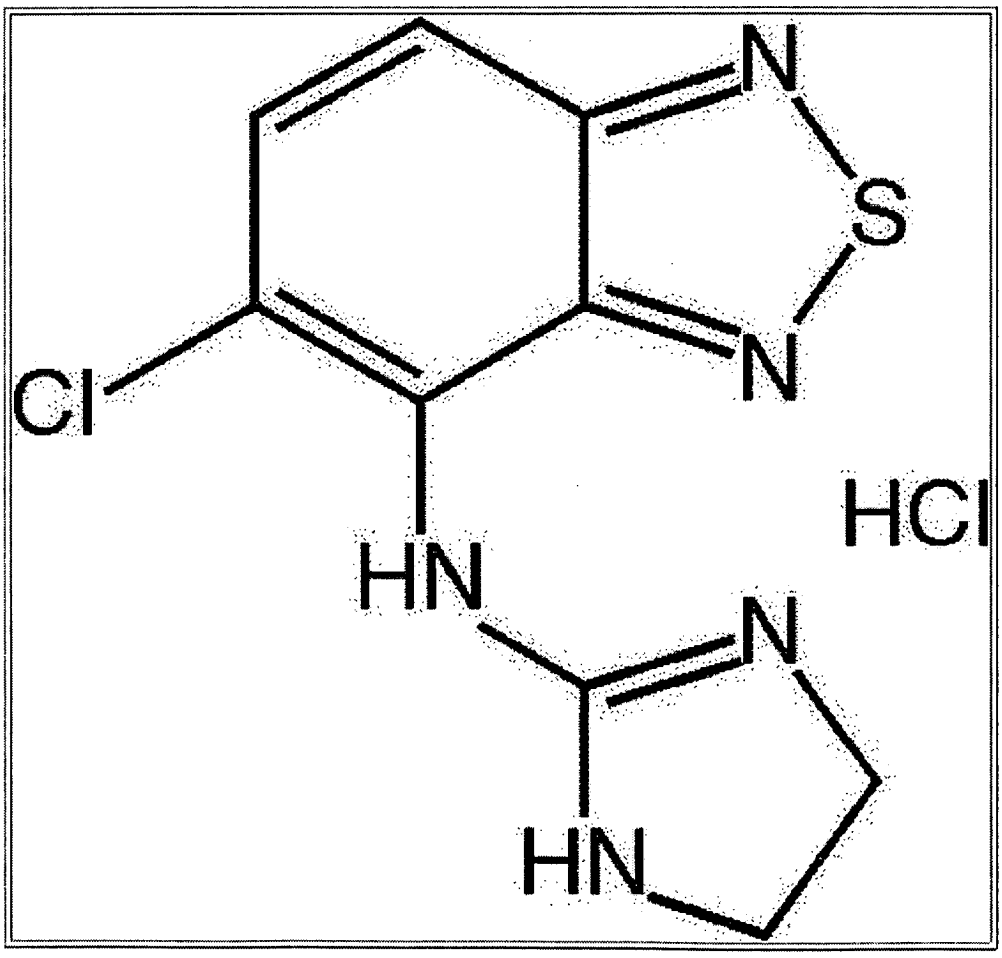
ZANAFLEX® (Elan)
(tizanidine hydrochloride)

Tablets 2 and 4 mg

Description

DESCRIPTION

ZANAFLEX * (tizanidine hydrochloride) is a centrally acting (alpha) $_2$ -adrenergic agonist. Tizanidine HCl (tizanidine) is a white to off-white, fine crystalline powder, odorless or with a faint characteristic odor. Tizanidine is slightly soluble in water and methanol; solubility in water decreases as the pH increases. Its chemical name is 5-chloro-4-(2-imidazolin-2-ylamino)-2,1, 3-benzothiodiazole hydrochloride. Tizanidine's molecular formula is $C_9H_8ClN_5S \cdot HCl$, its molecular weight is 290.2 and its structural formula is:



PDR® entry for

CATAPRES-TTS® (Boehringer Ingelheim)
(clonidine)

Transdermal Therapeutic System
Catapres-TTS® -1
Catapres-TTS® -2
Catapres-TTS® -3

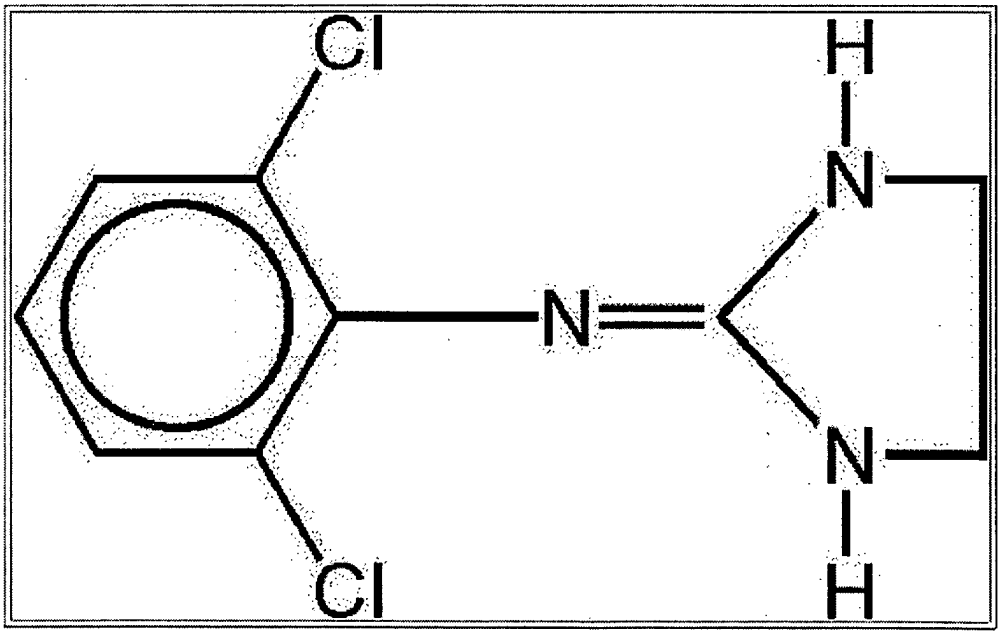
Description

Programmed delivery in vivo of 0.1, 0.2, or 0.3 mg clonidine per day, for 1 week.

Prescribing Information

DESCRIPTION

Catapres-TTS ® (clonidine) is a transdermal system providing continuous systemic delivery of clonidine for 7 days at an approximately constant rate. Clonidine is a centrally acting alpha-agonist hypotensive agent. It is an imidazoline derivative with the chemical name 2, 6-dichloro-N-2-imidazolidinylidenebenzenamine and has the following chemical structure:



(clonidine)

PDR® entry for

ULTRACET™ (Ortho-McNeil)
(tramadol hydrochloride/acetaminophen tablets)

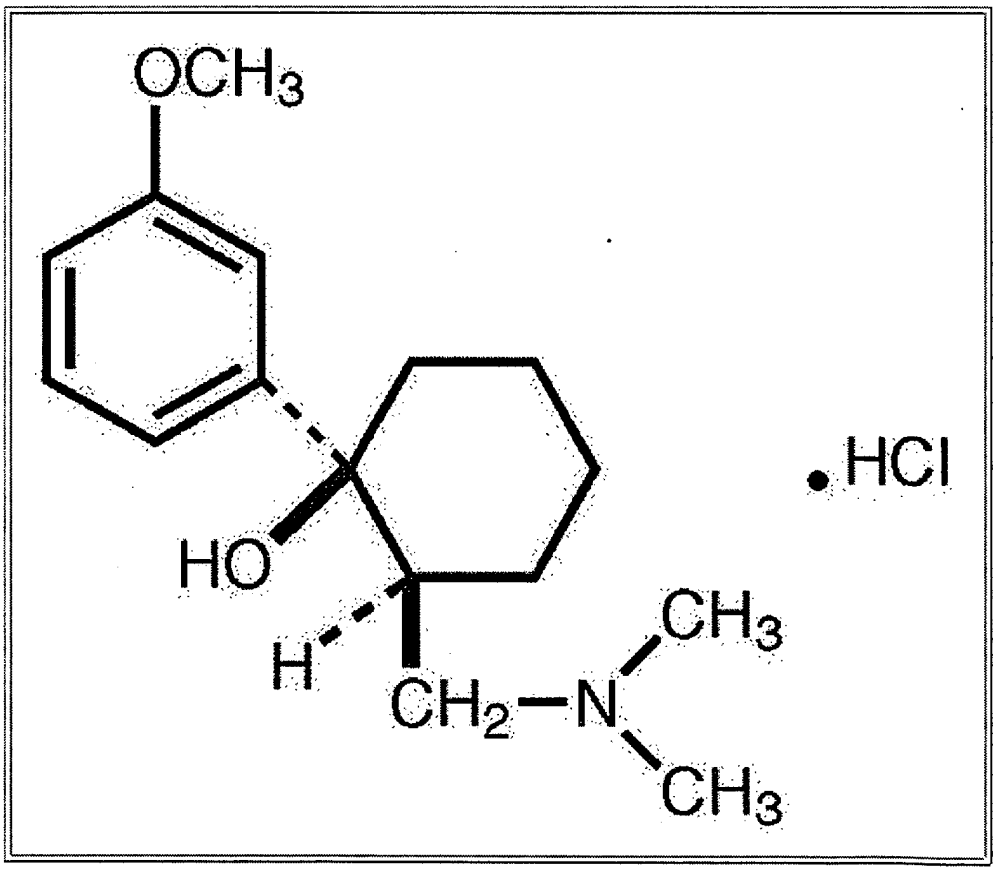
Description

Prescribing Information

DESCRIPTION

ULTRACET™ (37.5 mg tramadol hydrochloride/325 mg acetaminophen tablets) combines two analgesics, tramadol and acetaminophen.

The chemical name for tramadol hydrochloride is (±) *cis*
-2-[(dimethylamino)methyl]-1-(3-methoxyphenyl) cyclohexanol hydrochloride. Its structural formula is:



The molecular weight of tramadol hydrochloride is 299.84. Tramadol hydrochloride is a white, bitter, crystalline and odorless powder.

PDR® entry for

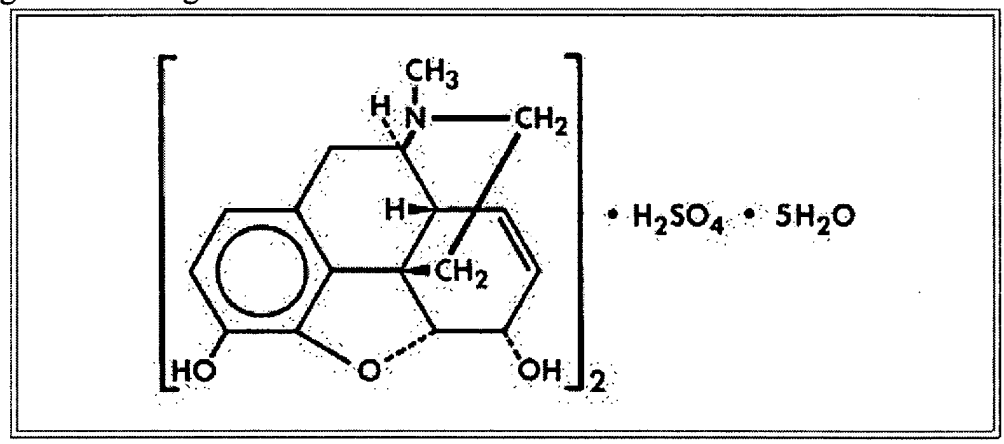
ASTRAMORPH/PF™ (AstraZeneca LP)

(morphine sulfate Injection, USP) Preservative-Free

Description

DESCRIPTION

Morphine is the most important alkaloid of opium and is a phenanthrene derivative. It is available as the sulfate, having the following structural formula:



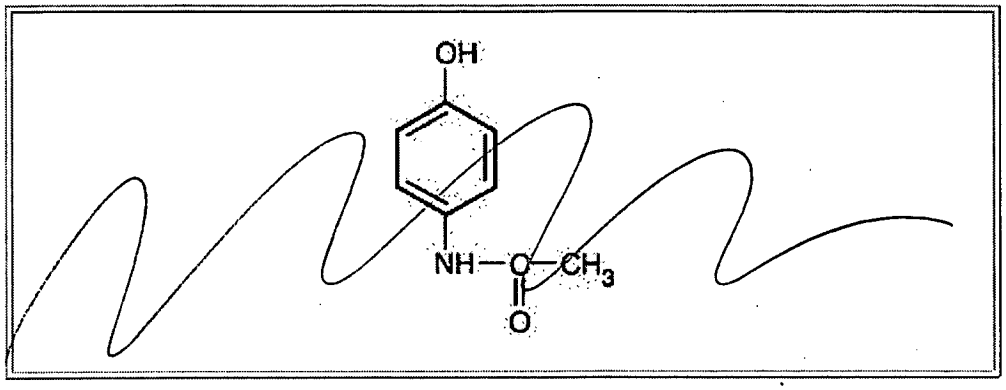
7,8-Didehydro-4,5-epoxy-17-methyl-(5(alpha),6(alpha))-morphinan-3,6-diol sulfate (2:1) (salt), pentahydrate

Preservative-free Astramorph/PF (morphine sulfate Injection, USP) is a sterile, pyrogen-free, isobaric solution free of antioxidants, preservatives or other potentially neurotoxic additives, and is intended for intravenous, epidural or intrathecal administration as a narcotic analgesic. Each milliliter contains morphine sulfate 0.5 mg or 1 mg (Warning: May Be Habit Forming) and sodium chloride 9 mg in Water for Injection. pH may be adjusted with hydrochloric acid to 2.5-6.5. Containers are sealed under nitrogen. Each container is intended for SINGLE USE ONLY. Discard any unused portion. DO NOT AUTOCLAVE.

(*back to top*)

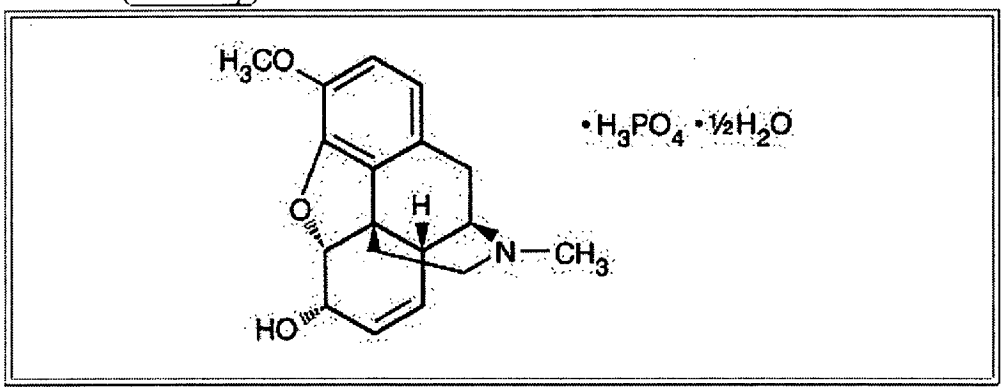
CLINICAL PHARMACOLOGY

Morphine exerts its primary effects on the central nervous system and organs containing smooth muscle. Pharmacologic effects include analgesia, drowsiness, alteration in mood (euphoria), reduction in body temperature (at low doses), dose-related depression of respiration, interference with adrenocortical response to stress (at high doses), reduction in peripheral resistance with little or no effect on cardiac index and miosis.



$C_8H_9NO_2$ M.W. 151.16

Codeine is an alkaloid, obtained from opium or prepared from morphine by methylation. Codeine phosphate occurs as fine, white, needle-shaped crystals, or white, crystalline powder. It is affected by light. Its chemical name is: 7,8-didehydro- 4, 5(alpha)-epoxy-3-methoxy-17-methylmorphinan-6(alpha)-ol phosphate (1:1) (salt) hemihydrate. Its structure is as follows: (*back to top*)



$C_{18}H_{21}NO_3.H_3PO_4.{}^1/_2H_2O$ M.W. 406.37

* See WARNINGS

(*back to top*)

CLINICAL PHARMACOLOGY

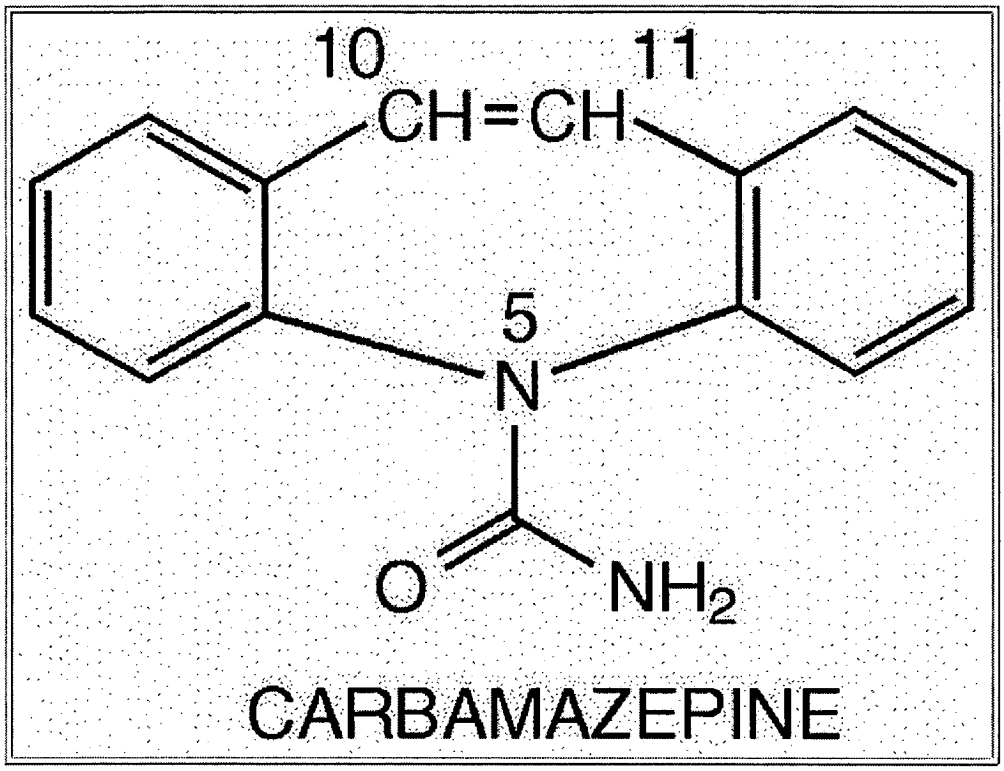
TYLENOL with Codeine (acetaminophen and codeine phosphate tablets and oral solution USP) combine the analgesic effects of a centrally acting analgesic, codeine, with a peripherally acting analgesic, acetaminophen. Both ingredients are well absorbed orally. The plasma elimination half-life ranges from 1 to 4 hours for acetaminophen, and from 2.5 to 3 hours for codeine.

Codeine retains at least one-half of its analgesic activity when administered orally. A reduced first-pass metabolism of codeine by the liver accounts for the greater oral efficacy of codeine when compared to most other morphine-like narcotics. Following absorption, codeine is metabolized by the liver and metabolic products are excreted in the urine. Approximately 10 percent of the administered codeine is de-methylated to morphine, which may account for its analgesic activity.

Acetaminophen is distributed throughout most fluids of the body, and is metabolized primarily in the liver. Little unchanged drug is excreted in the urine, but most metabolic products appear in the urine within 24 hours.

(*back to top*)

CARBATROL * is an anticonvulsant and specific analgesic for trigeminal neuralgia, available for oral administration as 200 mg and 300 mg extended-release capsules of Carbamazepine, USP. Carbamazepine is a white to off-white powder, practically insoluble in water and soluble in alcohol and in acetone. Its molecular weight is 236.27. Its chemical name is 5H-dibenz[b,f]azepine-5-carboxamide, and its structural formula is:



Carbatrol is a multi-component capsule formulation consisting of three different types of beads: immediate-release beads, extended-release beads, and enteric-release beads. The three bead types are combined in a specific ratio to provide twice daily dosing of Carbatrol.

Inactive ingredients: citric acid, colloidal silicon dioxide, lactose monohydrate, microcrystalline cellulose, polyethylene glycol, povidone, sodium lauryl sulfate, talc, triethyl citrate and other ingredients.

The 200 mg capsule shells contain gelatin-NF, FD&C Red #3, FD&C Yellow #6, Yellow Iron Oxide, FD&C Blue #2, and titanium dioxide, and are imprinted with white ink; and the 300 mg capsule shells contain gelatin-NF, FD&C Blue #2, FD&C Yellow #6, Red Iron Oxide, Yellow Iron Oxide, and titanium dioxide, and are imprinted with white ink.

(*back to top*)

CLINICAL PHARMACOLOGY

In controlled clinical trials, carbamazepine has been shown to be effective in the treatment of psychomotor and grand mal seizures, as well as trigeminal neuralgia.

Mechanism of Action

Carbamazepine has demonstrated anticonvulsant properties in rats and mice with electrically and chemically induced seizures. It appears to act by reducing polysynaptic responses and blocking the post-tetanic potentiation. Carbamazepine greatly reduces or abolishes pain induced by stimulation of the infraorbital nerve in cats and rats. It depresses thalamic potential and bulbar and polysynaptic reflexes, including the linguomandibular reflex in cats. Carbamazepine is chemically unrelated to other

PDR® entry for

MERIDIA® (Abbott)

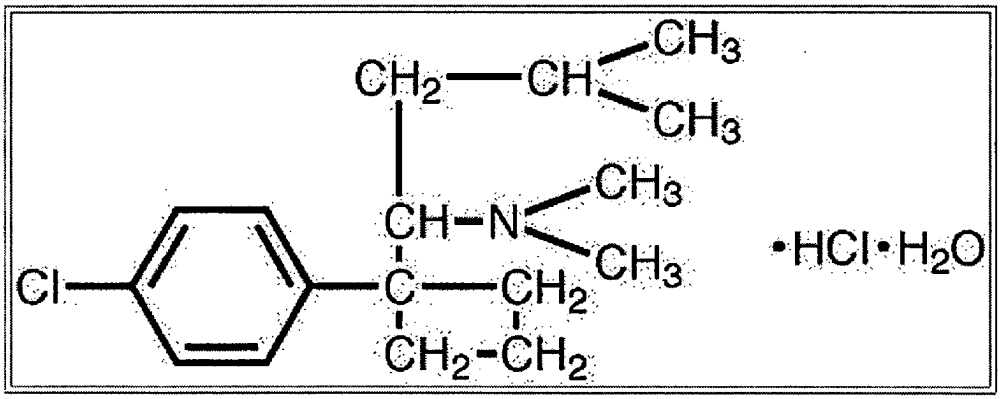
(sibutramine hydrochloride monohydrate) Capsules
Rx only

Description

DESCRIPTION

MERIDIA® (sibutramine hydrochloride monohydrate) is an orally administered agent for the treatment of obesity. Chemically, the active ingredient is a racemic mixture of the (+) and (-) enantiomers of cyclobutanemethanamine, 1-(4-chlorophenyl)- *N* , *N* -dimethyl-(alpha)-(2-methylpropyl)-, hydrochloride, monohydrate, and has an empirical formula of $C_{17}H_{29}Cl_2NO$. Its molecular weight is 334.33.

The structural formula is shown below:



Sibutramine hydrochloride monohydrate is a white to cream crystalline powder with a solubility of 2.9 mg/mL in pH 5.2 water. Its octanol:water partition coefficient is 30.9 at pH 5.0.

Each MERIDIA capsule contains 5 mg, 10 mg, 15 mg of sibutramine hydrochloride monohydrate. It also contains as inactive ingredients: lactose monohydrate, NF; microcrystalline cellulose, NF; colloidal silicon dioxide, NF; and magnesium stearate, NF in a hard-gelatin capsule [which contains titanium dioxide, USP; gelatin; FD&C Blue No. 2 (5- and 10-mg capsules only); D&C Yellow No. 10 (5- and 15-mg capsules only), and other inactive ingredients].

(*back to top*)

CLINICAL PHARMACOLOGY

Mode of Action

```
=> fil lreg
FILE 'LREGISTRY' ENTERED AT 13:27:04 ON 31 MAY 2002
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LREGISTRY IS A STATIC LEARNING FILE

=> d ide l1

L1   ANSWER 1 OF 1  COPYRIGHT 2002 ACS
RN   59-92-7  LREGISTRY
CN   L-Tyrosine, 3-hydroxy- (9CI)  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   Alanine, 3-(3,4-dihydroxyphenyl)-, L- (8CI)
OTHER NAMES:
CN   (-)-3,4-Dihydroxyphenylalanine
CN   (-)-Dopa
CN   .beta.-(3,4-Dihydroxyphenyl)-.alpha.-L-alanine
CN   .beta.-(3,4-Dihydroxyphenyl)-L-alanine
CN   .beta.-(3,4-Dihydroxyphenyl)alanine
CN   3,4-Dihydroxy-L-phenylalanine
CN   3,4-Dihydroxyphenyl-L-alanine
CN   3,4-Dihydroxyphenylalanine
CN   3-(3,4-Dihydroxyphenyl)-L-alanine
CN   3-Hydroxy-L-tyrosine
CN   DA
CN   Dihydroxy-L-phenylalanine
CN   DOPA
CN   Dopaflex
CN   Dopalina
CN   Dopar
CN   Dopaston
CN   Dopaston SE
CN   Eldopal
CN   Helfo-dopa
CN   Insulamina
CN   L-(-)-Dopa
CN   L-.beta.-(3,4-Dihydroxyphenyl)-.alpha.-alanine
CN   L-3-(3,4-Dihydroxyphenyl)alanine
CN   L-4,5-Dihydroxyphenylalanine
CN   L-DOPA
CN   Larodopa
CN   Levodopa
CN   Levopa
CN   Pardopa
FS   STEREOSEARCH
DR   25525-15-9, 23734-74-9, 72572-99-7, 72573-00-3, 90638-38-3, 88250-23-1,
     34241-25-3
MF   C9 H11 N O4
CI   COM
LC   STN Files:   ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS,
       BIOTECHNO, CA, CABA, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS,
       CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DIOGENES, DRUGU,
       EMBASE, GMELIN*, HODOC*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE,
       MRCK*, NAPRALERT, NIOSHTIC, PHARMASEARCH, PROMT, RTECS*, SPECINFO,
       SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL, VETU
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     Other Sources:   EINECS**, NDSL**, TSCA**, WHO
         (**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.
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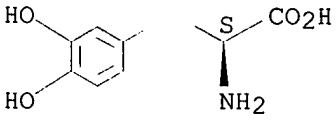
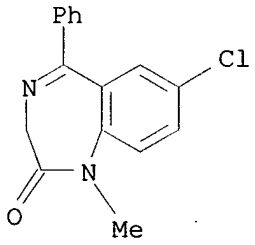


=> d ide l2

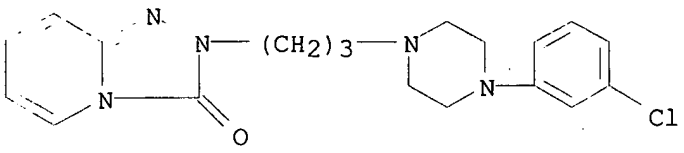
L2 ANSWER 1 OF 1 COPYRIGHT 2002 ACS
RN 439-14-5 LREGISTRY
CN 2H-1,4-Benzodiazepin-2-one, 7-chloro-1,3-dihydro-1-methyl-5-phenyl- (8CI, 9CI) (CA INDEX NAME)
OTHER NAMES:
CN 1-Methyl-5-phenyl-7-chloro-1,3-dihydro-1H-1,4-benzodiazepin-2-one
CN 1-Methyl-5-phenyl-7-chloro-1,3-dihydro-2H-1,4-benzodiazepin-2-one
CN 7-Chloro-1,3-dihydro-1-methyl-5-phenyl-2H-1,4-benzodiazepin-2-one
CN 7-Chloro-1-methyl-2-oxo-5-phenyl-3H-1,4-benzodiazepine
CN 7-Chloro-1-methyl-5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-one
CN 7-Chloro-1-methyl-5-phenyl-3H-1,4-benzodiazepin-2(1H)-one
CN An-Ding
CN Ansiolisina
CN Apaurin
CN Apozepam
CN Assival
CN Atensine
CN Atilen
CN Bialzepam
CN Calmocitene
CN Calmpose
CN Cercine
CN Ceregulart
CN Diacepan
CN Diapam
CN Diazemuls
CN Diazepam
CN Diazepam-Lipuro
CN Duxen
CN Eridan
CN Faustan
CN Horizon
CN LA 111
CN Lembrol
CN Levium
CN Methyldiazepinone
CN Methyldiazepinone (pharmaceutical)
CN Morosan
CN Noan
CN Org 2447
CN Paxate
CN Paxel
CN Quievita
CN Relaminal
CN Relanium
CN Ro 5-2807
CN Saromet
CN Seduxen
CN Setonil
CN Sibazon
CN Sibazone
CN Sonacon
CN Stesolid

CN Stesolin
CN Tranimul
CN **Valium**
ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT - Use FCN, FIDE, or ALL for DISPLAY
FS 3D CONCORD
DR 11100-37-1, 53320-84-6
MF C16 H13 Cl N2 O
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DETHERM*, DIOGENES, DRUGPAT, DRUGU, EMBASE, GMELIN*, HODOC*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC, PHAR, PHARMASEARCH, PIRA, PROMT, RTECS*, SPECINFO, TOXCENTER, TULSA, ULIDAT, USAN, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)



=> d ide l3

L3 ANSWER 1 OF 1 COPYRIGHT 2002 ACS
RN 19794-93-5 LREGISTRY
CN 1,2,4-Triazolo[4,3-a]pyridin-3(2H)-one, 2-[3-[4-(3-chlorophenyl)-1-piperazinyl]propyl]- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN s-Triazolo[4,3-a]pyridin-3(2H)-one, 2-[3-[4-(m-chlorophenyl)-1-piperazinyl]propyl]- (8CI)
OTHER NAMES:
CN Trazodon
CN **Trazodone**
FS 3D CONCORD
MF C19 H22 Cl N5 O
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CBNB, CEN, CHEMLIST, CIN, DDFU, DIOGENES, DRUGPAT, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, NIOSHTIC, PHAR, PHARMASEARCH, PROMT, RTECS*, SPECINFO, TOXCENTER, USAN, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)



=> d ide l4

L4 ANSWER 1 OF 1 COPYRIGHT 2002 ACS
RN 300-62-9 LREGISTRY
CN Benzeneethanamine, .alpha.-methyl- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Benzeneethanamine, .alpha.-methyl-, (.+-.)-
CN Phenethylamine, .alpha.-methyl-, (.+-.)- (8CI)
OTHER NAMES:
CN (.+-.)-.alpha.-Methylphenethylamine
CN (.+-.)-.alpha.-Methylphenylethylamine
CN (.+-.)-.beta.-Phenylisopropylamine
CN (.+-.)-1-Phenyl-2-aminopropane
CN (.+-.)-Desoxynorephedrine
CN (.+-.)-Phenylisopropylamine
CN .alpha.-Methyl-.beta.-phenylethylamine
CN .alpha.-Methylbenzeneethanamine
CN .alpha.-Methylphenethylamine
CN .alpha.-Methylphenylethylamine
CN .beta.-Aminopropylbenzene
CN .beta.-Phenylisopropylamine
CN 1-Benzylethylamine
CN 1-Methyl-2-phenylethylamine
CN 1-Phenyl-2-aminopropane
CN 1-Phenyl-2-propanamine
CN 1-Phenyl-2-propylamine
CN 2-Amino-1-phenylpropane
CN 3-Phenyl-2-propylamine
CN Actedron
CN Adderall
CN Adderall XR
CN Adipan
CN Allodene
CN Amfetamine
CN **Amphetamine**
CN Anorexine
CN Benzebar
CN Benzedrine
CN Benzolone
CN Desoxynorephedrine
CN dl-.alpha.-Methylphenethylamine
CN Elastonon
CN Fenopromin
CN Finam
CN Isoamyne
CN Isomyn
CN Mecodrin
CN Mydrial
CN Norephedrane
CN Novydrine
CN Obesin
CN Obesine
CN Oktedrin

CN Ortedrine
CN Percomon
CN Phenamine
CN Phenedrine
ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT - Use FCN, FIDE, or ALL for DISPLAY
FS 3D CONCORD
DR 60-15-1, 17108-96-2, 96332-84-2
MF C9 H13 N
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CHEMSAFE, CIN, CSCHEM, DDFU, DETHERM*, DIOGENES, DRUGU, EMBASE, GMELIN*, HODOC*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC, PHARMASEARCH, PIRA, PROMT, RTECS*, SPECINFO, TOXCENTER, USAN, USPAT2, USPATFULL, VETU
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Other Sources: DSL**, EINECS**, TSCA**, WHO
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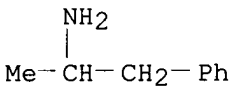
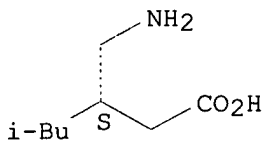


=> d ide

L5 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2002 ACS
RN 148553-50-8 REGISTRY
CN Hexanoic acid, 3-(aminomethyl)-5-methyl-, (3S)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Hexanoic acid, 3-(aminomethyl)-5-methyl-, (S)-
OTHER NAMES:
CN CI 1008
CN PD 144723
CN **Pregabalin**
FS STEREOSEARCH
MF C8 H17 N O2
CI COM
SR CA
LC STN Files: ADISINSIGHT, ADISNEWS, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CIN, DDFU, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, IPA, MRCK*, PHAR, PROMT, SYNTHLINE, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry. Rotation (+).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

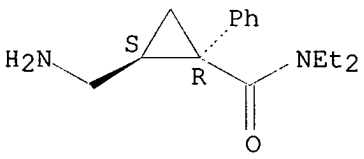
82 REFERENCES IN FILE CA (1967 TO DATE)
83 REFERENCES IN FILE CAPLUS (1967 TO DATE)

11 REFERENCES IN FILE CAPLUS (1967 TO DATE)

=> d ide 2

L6 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2002 ACS
RN 92623-85-3 REGISTRY
CN Cyclopropanecarboxamide, 2-(aminomethyl)-N,N-diethyl-1-phenyl-, (1R,2S)-rel- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Cyclopropanecarboxamide, 2-(aminomethyl)-N,N-diethyl-1-phenyl-, cis-(.+-.)-
OTHER NAMES:
CN Cyclopropanecarboxamide, 2-(aminomethyl)-N,N-diethyl-1-phenyl-, cis-
CN Midalcipran
CN **Milnacipran**
FS STEREOSEARCH
DR 105310-09-6
MF C15 H22 N2 O
CI COM
LC STN Files: ADISINSIGHT, ADISNEWS, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CBNB, CIN, DDFU, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, IPA, MEDLINE, MRCK*, PHAR, PROMT, SYNTHLINE, TOXCENTER, USAN, USPATFULL
(*File contains numerically searchable property data)
Other Sources: WHO

Relative stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

107 REFERENCES IN FILE CA (1967 TO DATE)
3 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
107 REFERENCES IN FILE CAPLUS (1967 TO DATE)

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=> fil reg; d ide
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STRUCTURE FILE UPDATES:   29 MAY 2002  HIGHEST RN 423115-51-9
DICTIONARY FILE UPDATES:  29 MAY 2002  HIGHEST RN 423115-51-9

TSCA INFORMATION NOW CURRENT THROUGH January 7, 2002

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Calculated physical property data is now available.  See HELP PROPERTIES
for more information.  See STNote 27, Searching Properties in the CAS
Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf


L6   ANSWER 1 OF 2  REGISTRY  COPYRIGHT 2002 ACS
RN   101152-94-7  REGISTRY
CN   Cyclopropanecarboxamide, 2-(aminomethyl)-N,N-diethyl-1-phenyl-,
     monohydrochloride, (1R,2S)-rel- (9CI)  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   Cyclopropanecarboxamide, 2-(aminomethyl)-N,N-diethyl-1-phenyl-,
     monohydrochloride, cis-(.+-.)-
OTHER NAMES:
CN   Cyclopropanecarboxamide, 2-(aminomethyl)-N,N-diethyl-1-phenyl-,
     monohydrochloride, cis-
CN   F 2207
CN   Milnacipran hydrochloride
FS   STEREOSEARCH
DR   86181-08-0
MF   C15 H22 N2 O . Cl H
SR   CA
LC   STN Files:   ADISINSIGHT, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CAPLUS, CIN,
       DRUGPAT, DRUGUPDATES, EMBASE, IPA, MRCK*, PHAR, RTECS*, SYNTHLINE,
       TOXCENTER, USPATFULL
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CRN  (92623-85-3)

Relative stereochemistry.
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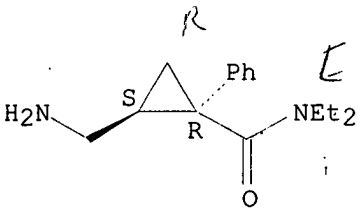

514/624

● HCl

11 REFERENCES IN FILE CA (1967 TO DATE)

Searched by Barb O'Bryen, STIC 308-4291

National Library of Medicine - Medical Subject Headings

2002 MeSH

MeSH Supplementary Concept Data

Return to Entry Page

Name of Substance	midalcipran
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CAS Type 1 Name	Cyclopropanecarboxamide, 2-(aminomethyl)-N,N-diethyl-1-phenyl-, cis-(+-)-
Entry Term	1-phenyl-1-diethylaminocarbonyl-2-aminomethylcyclopropane HCl
Entry Term	F 2207
Entry Term	F-2207
Entry Term	milnacipran
Heading Mapped to	*Cyclopropanes
Source	Neuropharmacology 1985;24(12):1211
Thesaurus ID	UD 37:235j
Pharm. Action	Antidepressive Agents
Pharm. Action	Serotonin Uptake Inhibitors
Pharm. Action	Adrenergic Uptake Inhibitors
Frequency	58
Note	structure given in first source
Date of Entry	19860404
Revision Date	20001212
Unique ID	C048107

Return to Entry Page